EXPLOITATION AND BIOMEDICAL
RESEARCH IN THE DEVELOPING WORLD

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The exploitation of participants is a significant problem in biomedical research, especially in the developing world. However, there is a gap between this problem and the theoretical literature on exploitation. This thesis will attempt to bridge it, considering Wertheimer and Sample’s theories. Whereas Wertheimer holds that exploitation is merely an unjust distribution of the “social surplus” arising from a transaction, Sample, whose approach this thesis endorses, construes exploitation as a lack of respect for a person’s true value. This thesis will show that codes of ethics with legal force take a Wertheimerian approach, and that the aspirational codes, which insist that research respond to local health priorities, are more Samplian. Finally, it will argue that the current system of research funding and oversight cannot guarantee that research is responsive to the needs of the developing world and thus fails to prevent exploitation.
RESUME

L’exploitation des sujets est un problème important dans la recherche biomédicale, surtout quand elle est menée dans les pays en voie de développement. Ce mémoire tentera d’appliquer la littérature théorique sur l’exploitation à ce problème, prenant en compte l’œuvre de Wertheimer et de Sample. Tandis que Wertheimer estime que l’exploitation n’est qu’une injustice dans la répartition du « surplus social » résultant d’une transaction, l’approche de Sample, dont ce mémoire approuve, envisage l’exploitation comme étant un manque de respect pour la valeur réelle de la personne. D’ailleurs, il démontrera que les codes d’éthique qui ont force légale ont tendance à être en accord avec Wertheimer, mais que ceux qui sont plutôt aspirionels incarnent certaines exigences d’inspiration Samplienne, par exemple, que la recherche réponde aux besoins de la communauté où elle est menée. Enfin, il démontrera que le système actuel de surveillance de la recherche ne peut pas garantir que cette condition soit respectée.
# LIST OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>45 CFR 46</td>
<td>U.S. Code of Federal Regulations Title 45 Human Welfare- Part 46 Protection of Human Subjects (also known as the Common Rule)</td>
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<tr>
<td>AZT</td>
<td>Azidothymidine, also known as Zidovudine</td>
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<tr>
<td>CDER</td>
<td>U.S. Center for Drug Evaluation and Research</td>
</tr>
<tr>
<td>CIHR</td>
<td>Canadian Institutes for Health Research</td>
</tr>
<tr>
<td>CIOMS</td>
<td>Council for International Organizations of Medical Sciences</td>
</tr>
<tr>
<td>CRO</td>
<td>Contract Research Organization</td>
</tr>
<tr>
<td>DHHS</td>
<td>The U.S. Department of Health and Human Services</td>
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<tr>
<td>FDA</td>
<td>The U.S. Food and Drug Administration</td>
</tr>
<tr>
<td>GCP</td>
<td>Good Clinical Practice</td>
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ICH
International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use

ICH-GCP Guideline
*ICH Harmonised Tripartite Guideline: Guideline for Good Clinical Practice E6(R1) (1996)*

IRB
Institutional Review Board

HIV
Human Immunodeficiency Virus

MTCT
Mother-to-child transmission

NBAC
National Bioethics Advisory Commission

NBAC Report
*Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries (NBAC 2001)*

NGO
Non-Governmental Organization

OHRP
The U.S. Office of Human Research Protections

OIG
The U.S. DHHS Office of Inspector General

REB
Research Ethics Board

REC
Research Ethics Committee

TCPS
*Tri-Council Policy Statement: Ethical Conduct for*
Research Involving Humans (Medical Research Council of Canada, Natural Sciences and Engineering Research Council of Canada, & Social Sciences and Humanities Research Council of Canada, 2003)

UNAIDS The Joint United Nations Programme on HIV/AIDS

UNAIDS Guideline Ethical Considerations in Preventive Vaccine Research (UNAIDS, 2000)

UNICEF The United Nations Children’s Fund

WMA World Medical Association
CHAPTER ONE: INTRODUCTION

The Trovan Scandal

In 1996, a meningitis epidemic was raging in Nigeria. According to reports, there were over 100,000 recorded cases and 11,717 deaths. About 84% of infections occurred in patients 20 years old or younger. Taming the epidemic required a colossal effort on the part of the Nigerian Ministry of Health, several U.N. agencies and a number of non-governmental organizations (NGOs) (Mohammed et al., 2000). In addition to these humanitarian groups, Pfizer, the American pharmaceutical giant, sent a team to Kano, Nigeria, but they had very different reasons for being there. Alongside a Doctors without Borders clinic, Pfizer established a research facility where they conducted a hastily-designed clinical trial of Trovan, an antibiotic. The children enrolled in the trial were assigned to either Trovan or Ceftriaxone. In some cases, the Trovan was administered parenterally, the approved route of administration, but in others it was given orally, a route that had never been tested in children before. There were also allegations of irregularities in the control group: in some cases children in the control group may have received sub-standard doses of Ceftriaxone. It is unclear whether this was done to manage side effects or to skew the results of the experiments in favour of Trovan.
Ultimately, 198 children were enrolled in the study. Eleven of them died and many more suffered debilitating injuries such as severe arthritis, blindness and lameness. Six weeks after they touched down, the Pfizer researchers had packed up and left (Stephens, 2000).

Although the children were not more likely to die in the trial than outside of it, there are many reasons to question the ethics of this study. In addition to testing an unproven form of the drug on desperate, vulnerable children, there were a number of ethical breaches. Firstly, the process of obtaining informed consent was grossly inadequate: there is no written record of consent, and the available evidence suggests that neither the children nor their parents understood even the basics of the study, or that it was being conducted for research purposes and not purely for the child’s benefit. Moreover, the protocol did not allow researchers to transfer patient-participants from the Trovan group to the Ceftriaxone group if they were not responding to the former, and indeed the diagnostic tests to determine whether they were responding were not performed in many cases. Finally, the Pfizer clinic diverted resources from the Doctors without Borders’ clinic, namely hospital beds that could have been used to provide standard, low-cost treatment (Stephens, 2000).

Thankfully, the Nigerian Trovan study is not representative of biomedical research in the developing world. Although there are many examples of misconduct, most are less flagrant. Nonetheless, the Trovan study illustrates many of the problems that may arise when research is conducted in developing countries. It shows that these populations, who may have little experience with medical care and even less with medical research, are extremely vulnerable. They may be so desperate for treatment that they are willing to accept any intervention. Although this particular study ended in failure, it shows that at
least one pharmaceutical company was willing to use this tragic situation to try and develop a commercial product. Finally it revealed the weakness of the ethics oversight mechanism in developing countries as it existed in 1996. While there are still ethical breaches in developed countries, there are few reports of such egregious treatment of research participants.

Exploitation: An Initial Definition

The elements just described—vulnerability, desperation, the opportunity to take advantage, and unfair treatment of the disadvantaged are some of the recurrent themes in the literature on exploitation. This thesis will examine the problem of exploitation in developing world research. As will become clear, exploitation is not a simple concept; nonetheless, an initial definition would be helpful. Alan Wertheimer, an often-cited authority on the subject, defines it as follows: “At the most general level, A exploits B when A takes unfair advantage of B.” Wertheimer calls this the “lowest common denominator definition” (1996, p. 10) and Arneson notes that there will “be as many competing conceptions of exploitation as theories of what persons owe to each other by way of fair treatment” (1992, p. 350). Thus, this definition masks the complexity of the concept, but it is adequate for this introductory chapter.
The Potential for Exploitation in Research

Much has been made of the different goals of medical care and research, and the need to hold them to different ethical standards. Although the distinction may be fuzzy in some cases, some generalizations can be made. In caring for their patients, physicians are bound to serve their patients’ interests. This is reflected in law, where the relationship is considered fiduciary, and in codes of ethics. For example, the Declaration of Geneva contains the unqualified statement, “A physician shall act in the patient’s best interest when providing medical care” (WMA, 2006). In contrast, the purpose of research is to produce generalizable knowledge in order to improve medical care for future patients. In many cases, this goal legitimately conflicts with the research participant’s best interests—research may involve risky procedures that have no compensating benefit for him or her.

Research that tests a therapeutic intervention is an interesting case: it fuses elements of the two activities. The patient-participant may reasonably expect a therapeutic benefit from the experimental intervention in some cases, though there may also be procedures and risks that have no therapeutic warrant. To complicate things further, this research may be sponsored by the manufacturer of the product, who stands to gain financially if it proves successful and many future patients may benefit from it. Taken together, these factors create the potential for exploitation in research.

The asymmetric relationship between physician-investigator and patient-participant may also contribute. The former are at an advantage in terms of technical knowledge and if they are unscrupulous, they could use this to their advantage. In addition, patients may feel a sense of obligation to their physicians, which could be used
to induce them to participate in research. Conversely, they may see their physician as gatekeepers and fear that their care may suffer if they decline to participate in research. Finally, research participants may not even appreciate the difference between research and care; they may mistakenly believe that all research procedures are done for their benefit, a phenomenon known as the therapeutic misconception (Appelbaum, Roth, Lidz, Benson, & Winslade, 1987).

These concerns are not merely theoretical: there have been many research scandals in the past century that could rightly be characterized as exploitative. For instance, in the Tuskegee Study of Untreated Syphilis, investigators observed the natural course of syphilis in 400 poor African American men between 1932 and 1972. The investigators responsible for this study went to great lengths to prevent participants from receiving treatment from any source and they were deceived in many ways over the course of the study. They were lied to about their diagnosis, and told that purely experimental procedures were in fact treatment (Tuskegee Syphilis Study Legacy Committee, 1996). Although this brief description of the study represents an oversimplification, a fuller description of the events is presented elsewhere (White, 2000) and it remains a paradigmatic case of exploitation in research.
The Heightened Potential for Exploitation in Developing Countries

Although the potential for exploitation is a constant concern in research, it is heightened when that research is conducted in developing countries. Emanuel, Wendler, Killen and Grady provide one reason why this is so:

In developed countries, the risk of exploitation of subjects or host communities is minimized, because society funds research to improve health, researchers and research institutions are part of the larger community, and there is an infrastructure, even if imperfect, that translates research results into health-care practices for the benefit of the larger community. Research in developing countries creates a greater risk of exploitation: individuals or communities in developing countries assume the risks of research, but most of the benefits may accrue to people in developed countries. (2004, p. 930)

While the lack of an adequate healthcare infrastructure contributes to the potential for exploitation, other historical factors play a role as well. For instance, regulatory changes in the United States have resulted in an increased demand for research participants and made it easier to use foreign data to support New Drug Applications (NDAs). This has lead to a rapid expansion in the volume of research occurring in such settings. Unfortunately, the ethical protection of human research subjects has not expanded at the same pace, leading to what Petryna has described as “ethical variability” (2006). In fact, the U.S. FDA officially removed any reference to the Declaration of Helsinki from the Code of Federal Regulations, replacing it with the requirement that
studies follow good clinical practice (GCP) (Human Subject Protection, 2008). Critics claim that this will further weaken the protections offered to research participants in the developing world. An editorial in Nature reads, “The FDA risks sending a message that ethical considerations are expendable when research subjects life half a world away” (Trials on Trial, 2008). Similarly, Kimmelman argues that this move is questionable in that it places too much emphasis on ICH-GCP, which has relatively little moral authority, it weakens the protections afforded to research participants, and it may even undermine the FDA’s stated goal of regulatory harmonization (2009).

“Ethical Variability” and Developing World Research

In her chapter entitled “Globalizing Human Subjects Research,” ethnographer Adriana Petryna (2006) documents the rapid expansion of biomedical research on human beings in developing countries in the mid-1990s and the “ethical variability” that has accompanied it. She claims that a number of factors came together to accelerate this off-shoring of clinical research. Firstly, the demand for human subjects grew dramatically at that time due to an increasing number of clinical trials and the need to conduct larger trials to satisfy regulatory authorities. Secondly, the American population was becoming less desirable as research participants due to “treatment saturation.” That is, research conducted with American participants was considered less reliable because they were taking too many other drugs, making it difficult to interpret the results. In contrast, participants in the developing world were more likely to be “treatment naïve,” making results more decisive. Petryna writes: “whatever an American is ready to provide as a
human subject, owing to a belief in scientific progress, altruism, or therapeutic need, will never be enough to satisfy the current level of demand for human subjects in commercial science” (p. 37). Finally, in the mid-1990s, the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) came into effect, facilitating the submission of results from foreign studies to the U.S. Food and Drug Administration (FDA).

To illustrate the dramatic effects of these developments, she cites a 2001 report from the U.S. Office of Inspector General. Its significant findings include a dramatic increase in the volume of foreign research under the FDA’s oversight. For instance, there was a 16-fold increase in the number of foreign investigators conducting research to be submitted to the FDA. In addition, it found that many of the foreign investigators were located in countries with limited experience conducting clinical trials. Finally, it found that the FDA was unable to ensure that participants were adequately protected in these settings, and that there was reason to believe that ethics committees in these areas were inexperienced and that they were not adequately monitoring ongoing research (OIG, 2001).

Petryna demonstrates that expansions in the ethical protections that are in place in developed countries have not kept pace with the expansion in research. She writes: “Pragmatic issues have overwhelmed ethics in terms of who controls international guidelines for ethical research and their capacity to protect the rights, interests, and well-being of human research subjects globally” (2006, p. 33). She is particularly critical of the International Conference on Harmonization’s (ICH) lax requirements regarding the use of placebos as controls. The ICH guideline reads:
Whether a particular placebo controlled trial of a new agent will be acceptable to subjects and investigators when there is known effective therapy is a matter of investigator, patient, and institutional review board (IRB)/independent ethics committee (IEC) judgment, and acceptability may differ among ICH regions. Acceptability could depend on the specific design of the trial and the patient population chosen. (2000, p. 14)

Although the Declaration of Helsinki is ambiguous on this matter, its requirement is stricter. It states that “The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods” (WMA, 2004). However, a “note of clarification” added in 2004 weakens this requirement stating that “However, a placebo-controlled trial may be ethically acceptable, even if proven therapy is available, under the following circumstances: Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method...” (WMA, 2004). Regardless of this ambiguity, there is evidence to suggest that the laxer ICH standard has prevailed. For instance, one study reviewed randomized controlled trials of interventions to treat HIV infection, Tuberculosis and Malaria conducted in sub-Saharan Africa between 1998 and 2003. It found that only 12 of 73 eligible trials provided participants in both the intervention and control arms treatment that met the best current clinical standards (Kent, Mwamburi, Bennish, Kupelnick, & Ioannidis, 2004).

It is clear from Petryna’s observations that the stage is set for exploitation. She notes that contract research organizations (CROs) compete intensely for research subjects, writing that “currently there is a turf war raging among pharmaceutical sponsors
for human subjects. The competition is not only about the number of subjects a given company can recruit, it is also about recruiting subjects quickly” (2006, p. 40). In addition, potential participants in these countries may be particularly desperate and vulnerable, as the healthcare otherwise available to them, if any, may be of poor quality. Finally, if there is not proper oversight by an ethics committee, it is more likely that participants will be coerced or deceived.

Petryna also documents the pharmaceutical industry’s defence of their off shoring practices. She writes, “This move may appear exploitative, but the pharmaceutical industry argues that it is positive because in these regions clinical trials have become social goods in themselves” (2006, p. 41). This defence, however, is rooted in the assumption that if the participant or the community benefits, the interaction cannot be exploitative. However, Chapter Two will challenge that assumption, arguing that exploitation can in fact be mutually advantageous.

**Outline of this Thesis**

This thesis explores the concept of exploitation as it relates to biomedical research, particularly in the developing world. Chapter Two will consider three influential theories of exploitation. Firstly, it will examine that of Robert Goodin, “Exploitation as Vulnerability,” arguing that it is internally inconsistent, but that some of Goodin’s commentary adds to an analysis of exploitation in research. Next it will consider Alan Wertheimer’s market-based theory of exploitation. It will argue that although Wertheimer has identified an important category of exploitative transactions, his
theory fails to account for all instances of exploitation. If, as Wertheimer suggests, exploitation only occurs in the context of a transaction, it follows that only parties to the transaction can be exploited, and that the only grounds for a claim of unfairness lies in the distribution of the “social surplus” arising from the transaction. Using examples from developing world research, I will show that this is untenable. Finally, it will examine Ruth Sample’s “Exploitation as Degradation.” I will argue that Sample offers the most satisfactory theory of exploitation, in that it accounts adequately for the wrongness of exploitation, provides criteria for distinguishing between exploitative and non-exploitative interactions and accounts for a broad range of research that instinctively seems exploitative.

Chapter Three will analyze selected codes of ethics for biomedical research in light of the discussion in Chapter Two. It will argue that some codes of ethics, particularly those that are seen as aspirational rather than pragmatic, go beyond Alan Wertheimer’s narrow conception of exploitation and embrace some of Sample’s ideals. This includes provisions that require research to be responsive to local health needs and that the fruits of research be made reasonably available to the populations in which it was conducted. However, codes of ethics that are more pragmatic and have more legal or regulatory force tend to be more Wertheimerian in their approach.

Chapter Four will describe the current mechanisms of research funding and ethics oversight. It will argue that funding mechanisms in both the public and private sectors lead to research that is oriented towards diseases that are prevalent in the developed world and treatment regimens that are viable there. Therefore, such research is not representative of local health needs and qualifies as exploitative in Sample’s sense of the
word. The current model of ethics oversight involves an institution-by-institution, protocol-by-protocol review of research, which cannot prevent such exploitation.

Chapter Five will provide a summary and conclusion. In addition, it will go beyond the negative obligation of avoiding exploitation, summarizing some of the literature on the positive goals towards which research should strive.

A Note on Terminology

The terms “developing” and “developed” are somewhat slippery and I would like to clarify my use of them here. I will use the terms “developed countries” and “developed world” to refer to the 25 OECD member countries that are classified as high-income by the World Bank. I will use the term “developing countries” to refer to countries classified as low-income, lower middle income and upper middle income economies. I acknowledge that this classification is imperfect, and especially that it does not do justice to the differences between developing countries. Nonetheless, this distinction is meaningful in that the world’s largest research-based pharmaceutical companies are all based in high income countries and the vast majority of public funds for health research are granted by these countries. Furthermore, I realize that the terms “developed” and “developing” are loaded: they imply that economic development is a proper measure of a country’s standing. Moreover, the term “developing” may be overly optimistic in some cases: some of these countries have experienced economic and social decline in recent years. Nonetheless, I will use these terms here.
It is widely accepted that research should be reviewed for ethics by an independent body before it begins. However, the terminology for these bodies varies from jurisdiction to jurisdiction. They are called Research Ethics Boards (REBs) in Canada, Institutional Review Boards (IRBs) in the U.S. and Human Research Ethics Committees in Australia. I will use the term Research Ethics Committees and the abbreviation REC to refer to all such bodies.

The terms used to describe those who are enrolled in medical research are also controversial. One sometimes hears them referred to as “patients,” “participants,” and “subjects.” Here, I will only use the term “patients” to describe individuals who are receiving medical care. Such people may also participate in medical research- I will call them “patient-participants” where appropriate. It is also possible for an individual to be a part of medical research without receiving any medical care- I will use the term “participants” to refer to them. I dislike the term “subjects” as it seems to imply that they are the mere object of an experiment and that they do not have an active role to play in deciding to be involved in research and in adhering to study procedures. In general, I will avoid it.
CHAPTER TWO: THEORIES OF EXPLOITATION

Introduction

This chapter will examine a number of theories of exploitation with a view to an ethical analysis of developing world research. Ideally, a theory of exploitation would specify necessary and sufficient conditions and allow us to classify different interactions or relationships as exploitative or not exploitative. While such a theory may challenge our intuitions about some cases of exploitation, it should not stray too far from our everyday usage of the term. Moreover, it would be internally consistent, explain what is morally wrong about exploitation, and provide insight into the moral force of exploitation. Finally, it would clearly specify what groups can be the objects of an exploitation claim, that is, who can exploit and who can be exploited. This chapter will argue that Goodin’s “Exploitation as Vulnerability” fails in that it is internally inconsistent, but nonetheless contributes to our understanding of exploitation. Sample and Wertheimer offer theories that come close to meeting these conditions, though overall Sample’s is superior in most respects. Wertheimer construes exploitation as a micro-level phenomenon that occurs in the context of a transaction, typically a transaction between individuals, and his only criterion for exploitativeness is an unfair distribution of the benefits arising from the transaction. His prototypical example of an exploitative interaction is a commercial transaction in which one party manages to obtain a non-market price for the goods in question. I will argue that although transactions in which the distribution of benefits is
unfair constitute one type of exploitation, this paradigm is ill-suited to an analysis of exploitation in research. Sample’s theory of exploitation, which views exploitation as degradation is better adapted to an ethical analysis of research participation. She understands degradation to mean treating a person as if they were worth less than they really are. This can happen if an interaction is insufficiently attentive to one party’s flourishing and well-being, if an interaction takes advantage of a past injustice, or if an interaction commodifies an aspect of a person that should not be commercialized. Although Sample’s typical examples of exploitation involve individuals, her theory can easily be extended to account for exploitation of larger groups such as communities.

**Why Theorize?**

Exploitation is a recurring theme in the research ethics literature. Fitzgerald and Wasunna suggest that non-exploitation has become the central principle in the field. They write, “Just as one of the principles underlying the Hippocratic Oath is ‘First, do no harm,’ a principle underlying medical research ethics may be, ‘First, do not exploit’” (2005). This may not be an exaggeration. For instance, in their influential article, “What Makes Clinical Research Ethical?” Emanuel, Wendler and Grady write, “Ethical requirements for clinical research aim to minimize the possibility of exploitation by ensuring that research subjects are not merely used, but are treated with respect while they contribute to the social good” (2000, p. 2701). Similarly, Udo Schüklenk writes, “Research ethics are essentially about ways to ensure that vulnerable people are protected from exploitation and other forms of harm” (2000, p. 969). Miller and Brody have even
explicitly argued that non-exploitation ought to replace equipoise as the guiding principle for randomized clinical trials. They write:

We contend, by contrast, that the endorsement of clinical equipoise renders incoherent any account that arises from the difference position. The most important next step for research ethics is to develop this “non-exploitation” framework systematically in a way that avoids any conflation of clinical research with medical care. (2003, p. 19)

Finally, the Nuffield Council Report lists the duty to avoid exploitation as a central principal guiding the ethics of developing world research (2002). If this is truly the trend in research ethics, a correct account of the concept would be useful.

On the other extreme, there are those who insist that exploitation is useless as a tool for moral criticism. For instance, Robert Temple of the FDA’s Center for Drug Evaluation and Research (CDER) is quoted as saying, “Exploitative is a word better omitted from this document. It’s just a cuss-word, with no clear meaning or useful purpose” (Macklin 2004, p. 109). Although I strongly disagree with Temple’s comment, it points to the fact that the concept is often used too casually. Even Ruth Macklin, who draws extensively on the concept, notes that, “It may be easier to recognize exploitation when we see it than to define the concept” (2004, p. 99). Alan Wertheimer also acknowledges this. He writes:

Despite the frequency and ease with which we make exploitation claims in ordinary moral and political discourse, I think it is fair to say that with the... exception of the Marxist tradition, exploitation has not been a central concern for contemporary political and moral philosophy. (1996, p. 6)
A thorough examination of the concept will sharpen it as a tool for moral criticism.

Another reason to thoroughly examine the theoretical literature on exploitation is that many codes of ethics attempt to provide guidance on avoidance of exploitation, some explicitly, others implicitly. However, many of these codes were promulgated in response to particular instances of exploitation. Consequently, they may embody too narrow a conception of exploitation, and may not be well-adapted to exploitation that occurs in new and different circumstances. As Emanuel, Wendler and Grady write,

By focusing on the instigating issues, these guidelines tend to emphasize certain ethical requirements while eliding others. For instance, The Nuremburg Code... focused on the need for consent and a favourable risk-benefit ratio but makes no mention of fair subject selection or independent review. (2000, p. 2702)

Considering how much weight is being placed on the principle of non-exploitation, one would think that its theoretical underpinnings would be firmly established. However, this does not appear to be the case. Although there is a growing literature on exploitation in research, few articles take the time to explore the concept in any depth. Moreover, some articles cite Alan Wertheimer as their only authority on exploitation\(^1\), thereby ignoring differing conceptions of it.

\[^1\text{In addition to the works just cited, see Resnik (2003), Macklin (2004) and The Participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries (2004), Ballantyne (2005), Emanuel Wendler and Grady (2000) and Gbadegesin & Wendler (2006).}\]
One might argue that the discussion that follows is entirely semantic, that some people mean one thing by exploitation and others mean something different. However, the different theories of exploitation discussed here differ not only in their criteria for exploitation, but in their concept of why exploitation is wrong. Thus, it is not merely a matter of which interactions are included and which are excluded, but of what is morally wrong with such interactions. Perhaps it would be more precise to have different terms for the concepts described by Goodin, Wertheimer and Sample; at the very least one should appreciate the differences between them and specify which version one is invoking when making an exploitation claim.

This thesis excludes any discussion of Marxist exploitation which is certainly the most mature theory on the subject. A Marxian analysis in the context of research might have been interesting. Marx’s work focuses on labour and exploitation of the working class by capitalists and frames the problem in technical economic terms. Nonetheless, the analogy between labour and research participation seems plausible, especially in some developing world research. A labourer alienated from the product of his or her work might be seen as analogous to the research participant who does not have access to a successfully tested product at the end of a study. However, the moral dynamics of the relationship between the physician-investigator and patient-participant are very complex and Marxist analysis might not be able to capture this. Unfortunately, although there have been Marxist analyses of assisted suicide (Lester, 2002), organ sales (Hughes, 1998), reproductive technologies (Gimenez, 1991) and the “commodification” of healthcare (Caplan, 1989), to my knowledge there are no published Marxist analyses of the exploitation in research. This would mean starting such an analysis from scratch and
considering the volume and complexity of Marx’s work it would be beyond the scope of a Bioethics Master’s thesis.

**Some Common Ground**

Chapter One offered a “lowest common denominator” definition of exploitation: “At the most general level, A exploits B when A takes unfair advantage of B” (Wertheimer, 1996, p. 10). Neither Sample nor Goodin object to this. Moreover, the three theories share the same notion of “taking advantage.” They agree that “advantage” has two distinct senses— it can mean either a superior position or greater well-being. “Taking advantage” means using the former to obtain the latter. Thus, an exploitative interaction is one in which A becomes better off through his, her or their interaction with B. In addition, they agree that exploitation can be mutually advantageous. In contrast, some commentators claim that an interaction is only exploitative if it results in some harm to the exploitee. For example, Allen Buchannan claims that, “to exploit a person involves the harmful, merely instrumental utilization of him or his capacities, for one’s own advantage or for the sake of one’s own ends” (1985, p. 87). However, this does not square with our usual understanding of the word, and the theorists surveyed here all acknowledge that an interaction from which both parties benefit can still be exploitative.

A minor area of disagreement is whether an interaction in which A attempts but fails to make him- or herself better off should be considered exploitative. While some commentators claim this is merely “attempted exploitation,” for reasons that will be discussed, such cases will be counted as full-blown exploitation here.
Thus, the major disagreements between these theories revolve around their concepts of unfairness. They disagree on the importance of deception or coercion, the role of power dynamics and vulnerability and on the nature of the criteria that should be used to discriminate between exploitive and non-exploitive interactions. Some theories take a “historical” approach, meaning that the process leading up to an interaction constitutes exploitation; others take a “patterned” approach, meaning that it is the outcome of the transaction that matters. Ultimately, it is these factors that distinguish the theories.

**Goodin: Exploitation as Vulnerability**

*An Overview of the Theory*

Goodin’s theory of exploitation hinges on the duty to protect the vulnerable. Indeed he claims that the notions of vulnerability and exploitation are analytically inseparable. He writes, “Just as the notion of adultery is parasitic upon the notion of a ‘duty of marital fidelity’ (it is defined as, and its wrongness traced wholly to, the violation of that duty), so too with the notion of ‘exploitation’ and protecting the vulnerable” (1988, p. 188). In fact, he goes so far as to claim that vulnerability is the main source of our moral obligations (1985). This is quite unusual; the conventional wisdom is that our moral obligations flow from many sources, such as promises we have made and special relationships we are part of. Goodin subsumes these as special cases of vulnerability. He lists three necessary conditions for vulnerability: first, *needing* (and not
just wanting) a particular good; second, depending on a particular person for that good; and third, that person having discretionary control over it. He claims that the person in control has a duty to provide for the person in need because doing so will bring about positive consequences for him or her. He writes, “Vulnerability amounts to one person’s having the capacity to produce consequences that matter to another” (1985, p. 114; emphasis added).

According to Goodin, the duty to protect the vulnerable has two components. Firstly, it involves an obligation to actively protect the interests of vulnerable people, and to prevent others from adversely affecting their interests. He notes that defaulting on this obligation would be a “mere failure to discharge” (1988, p. 187). Secondly, it involves an obligation to suspend the ordinary rules of behaviour when dealing with vulnerable people. The ordinary rules of behaviour, he claims, allow us to “play for advantage” in many situations, but when the other party is vulnerable, it is no longer acceptable to do so. This is what Goodin defines as exploitation: playing for advantage when the other party is vulnerable.

Goodin claims that there are four categories of situation in which it is inappropriate to play for advantage (1988, p. 185). Firstly, it is inappropriate when the other party, for example a close friend, has renounced playing for advantage. Secondly, it is inappropriate when the other party is “unfit or otherwise unable to play in games of advantage at all.” Thirdly, it is inappropriate when the other party is grossly outmatched. And fourthly, it is inappropriate when one party’s advantage stems from the other’s grave misfortune. Though these situations differ greatly, they all result in one party being vulnerable to the other.
With that said, it is worth noting some considerations that he rejects as criteria for defining exploitation. Firstly, some claim that a transaction is exploitative only if the exploitee is coerced or forced into it\(^2\). Goodin counters that exploitation between intimates is still exploitation, even when there is no threat of force. Secondly, he discounts the notion that exploitation can be reduced to a certain kind of lack of reciprocity. Here, he uses a counterexample in which a person charged an unfairly high price for something because that person failed to bargain with the seller to achieve a fair price. Such a transaction would lack reciprocity it would not be considered exploitative. Thirdly, he rejects manipulation as a necessary condition for exploitation. Manipulation, he claims, must be active, deceptive and contrary to the will of the exploitee. However, he shows that in many transactions that we consider exploitative, the exploiter neither manipulates circumstances to his or her advantage nor deceives the exploitee. For instance, when a sweatshop owner pays his or her employees the standard subsistence wage, he or she is merely passively using an unfortunate situation, not manipulating the situation to his or her advantage. Likewise, when an oligopoly manipulates supply to drive prices up, it sometimes does so in plain view. Thus, exploitation can be neither active nor deceptive, so manipulation cannot serve as a criterion for exploitiveness.

\(^2\) For example, according to Moore, “… exploitation forms part of an exchange of goods and services when 1) the goods and services exchanged are quite obviously not of equivalent value, and 2) one party to the exchange uses a substantial degree of coercion” (1973, p. 53).
A General Critique

Goodin’s theory of exploitation appears compelling at first. His emphasis on vulnerability appears sound, as in most exploitative transactions, the exploitee is in fact vulnerable in some way. It provides an account of the wrongness of exploitation and gives criteria to determine whether a particular transaction is exploitive or not. Goodin’s argument that exploitation is only morally offensive when the goods in question are something the exploited party needs is quite insightful. On closer inspection though, there are at least three major problems with the theory.

Firstly, Exploitation as Vulnerability suffers from serious internal tensions. Goodin gives a historical account of the wrongness of exploitation, as opposed to a patterned account. Indeed he explicitly insists on it. He writes, “The essence of exploitation must be sought in some characteristic of the process, rather than in some characteristic of the end results” (1987, p. 181). Specifically, exploitation is wrong because the exploiter violated the norm of protecting the vulnerable. However, Goodin also claims that this duty arises because one person is in a unique position to improve the other’s situation, that is, to produce positive consequences for that person.

His argument might be summed up as follows:

1) Everyone has a duty to protect the vulnerable. This duty entails not exploiting them, that is, not playing for advantage against them.

2) Everyone has a duty to protect the vulnerable because doing so produces positive consequences for them.
This argument cannot logically account for mutually advantageous exploitation. It is not logically problematic when both conditions are met, that is, when we protect the vulnerable and positive consequences result, or when we fail to protect the vulnerable and negative consequences result. Nor is it especially problematic when we protect the vulnerable, but negative consequences nonetheless come about. We routinely accept that the consequences of our actions are not fully predictable, and that even when we do our duties, bad things happen. However, it is problematic in the situation where we do not protect the vulnerable (i.e., we play for advantage against them) but the vulnerable party nonetheless benefits. This is the case in mutually advantageous exploitation. Here, it is no longer clear why we must not play for advantage against the vulnerable, because interactions in which we do play for advantage can nonetheless benefit the weaker party. Sample phrases this critique as follows:

Goodin says that exploitation can occur when both parties benefit but some norm of interaction for “unusual circumstances” is violated. But if, as he also says, his view is fundamentally consequentialist, this raises the question of what is morally wrong with a transaction that improves the situation of all those involved, no matter how unusual the transaction.

(2003, p. 51)

Clearly, Goodin’s argument and my criticism of it hinges on the fiction that incommensurate entities can be added and subtracted to produce a net increase or decrease in well-being. It supposes, for example, that money and health might be added and subtracted from one another. This is a general problem in utilitarian ethics and I will
not comment on it further except to say that individuals often face these trade-offs but nonetheless manage to make decisions that are consistent with their long-held beliefs.

Secondly, Goodin’s theory suggests that playing for advantage is all-or-nothing: either we do play for advantage or we don’t. In reality, the advantage one extracts from an interaction is a matter of degree. One could argue then, that the duty not to play for advantage is also a matter of degree, and that only at a particular point does playing for advantage become exploitative. However, this would require that we have a way of determining where that point lies, but Goodin does not provide such a mechanism.

Thirdly, “Exploitation as Vulnerability” overuses the notion of “playing for advantage.” Although this notion is consistent with our everyday understanding of exploitation, it is nonetheless problematic in three ways. For one, the phrase “playing for advantage” seems to imply an active process, but elsewhere Goodin insists that exploitation need not be active. (Recall the sweatshop owner who pays his or her employees the unfairly low subsistence wage.) This phrase is also problematic in that it seems very broad. It could mean simply profiting from a transaction, or it might mean conniving to maximize one’s own benefits at the expense of one’s interactor. This is quite a broad spectrum of behaviour. Ordinarily, it would seem that there is nothing wrong with profiting from a transaction if it is fair to the vulnerable party. However, conniving to extract as much as possible from a vulnerable person seems most unethical. Unfortunately, to my knowledge Goodin never explicitly defines the phrase, though he does note that what counts as fair play depends on the nature of the game (1987, p. 183). Finally, it is problematic in that it appears to make the exploiter’s motivations a criterion for exploitation from a regulatory point of view. That is, the fact that A has obtained a
benefit from the interaction is not sufficient. A must actively, consciously pursue an advantage for it to be exploitation; for example, A must opt into the putatively exploitive interaction because of some perceived advantage to him- or herself. This is problematic in three ways. Firstly, it is difficult to determine what a person’s motivations are, so it would be difficult to apply the “playing for advantage” criterion in practice. Secondly, the effect on B may be the same, regardless of what A’s intentions are. Finally, if transactions are only exploitative when one party plays for advantage, it seems to exclude exploitative interactions that are so culturally entrenched that few people question them. In this situation, the exploiter merely has to engage in socially accepted practices to gain an advantage, but does not have to actively play for it. Thus, the notion of “playing for advantage” would need to be explored further if it is to be of any use in the analysis of exploitation.

Application to Research

Goodin situates the wrongness of exploitation in the potential for producing positive consequences for vulnerable parties. This creates an internal inconsistency with respect to mutually advantageous exploitation. As discussed above, this is an important theoretical problem but it need not be fatal in the context of research. In research ethics there is a long tradition of protecting the vulnerable, though it is rooted in the principle of respect for persons, as opposed to consequentialism. For instance the Belmont Report declares that, “Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with
diminished autonomy are entitled to protection” (The National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research, 1979). Thus, the remainder of Goodin’s theory may make valuable contributions to our understanding of exploitation in research.

However, another weakness is the imprecision of the term “playing for advantage.” In addition to the criticisms mentioned above, it implies that the two parties are in an adversarial relationship with one another, but this is often not the case in research. Most often, investigators do not “play for advantage” over their research participants. Indeed, they may be doing their work for the good of humanity (or more mundane reasons, like getting paid or advancing their careers). Ideally, the physician-investigator and the patient-participant can be considered collaborators with a common goal (Jonas, 1969). If this is the case, the language of “playing for advantage” seems out of place, even though exploitation may still occur in such a relationship.

However, research involves many parties, including patients, investigators, sponsors, granting agencies, host countries and institutions, and each of these has its own agenda when engaging in research. Goodin’s theory fails to account for this as they consider exploitation only in bilateral relationships. In reality, research and most other interactions occur within a web of relationships.

The phrase “playing for advantage,” does describe some interactions in research aptly though. There are clear cases where sponsors and especially CROs are playing for advantage, though perhaps not directly against research participants. This is clear from the language they use to describe recruiting participants. For instance, a veteran recruiter interviewed by Adriana Petryna is quoted as saying,
It’s a question of how many patients I can get within a limited area, which reduces travel costs... Treatment-naïve populations are considered ‘incredibly valuable’ because they do not have any background medication... or any medication, for that matter, that might confuse the results of the trial. (2006, p. 41)

Thus, despite the imprecision of the term it would seem that some parties involved in research are playing for advantage.

Nonetheless, Goodin’s theory provides some interesting insights into exploitation in the context of research. In particular, Goodin’s categories of people that should be thought of as vulnerable mesh well with some widely held views in bioethics and his framing of these categories yields valuable insights into the wrongness of playing for advantage against these groups.

For example, he claims that it is inappropriate to play for advantage when the other party has renounced playing for advantage. Although Goodin envisions this as accounting for exploitation between intimates such as close friends or spouses, it applies well to research participants as well. Research participants may hope to gain from their participation in research but they are typically not “playing for advantage” in the sense that Goodin uses the phrase. To the contrary, much like the spouse who trusts his or her partner not to use the relationship unfairly, research participants place a great deal of trust in physician-investigators. The physician-investigator in turn has an obligation not to abuse that trust, for example by keeping a participant on a trial if it becomes clear that this is not in his or her best interests. This may not be the most advantageous course of action for the investigator (for example because the study will be more scientifically valid
if more participants complete it), but his or her first duty is still to the patient-participant\(^3\). It should be noted that there is some debate in the literature as to whether the relationship between physician-investigator and patient-participant is legally a fiduciary relationship, or something less than that (Miller & Weijer, 2006; Richardson & Belsky, 2004). Still, no one would claim that investigators may completely disregard participants’ interests and maximize their own benefits.

Similarly, his argument that it is inappropriate to play for advantage against those who are “grossly outmatched” or those who are “unfit to participate in the game,” applies well in the research context. Although the analogy with game-playing is tenuous, as discussed above, the relationship between physician-investigator and patient-participant is usually highly asymmetric, with the former holding most of the power. This power might stem from his or her extensive knowledge of the patient-participant’s condition and the range of treatments available to treat it. This means that the unscrupulous physician-investigator could deceive his or her patient to induce him or her to participate in research, even though this is universally regarded as unethical. The power might also stem from the physician-investigator’s perceived or real position as the gate-keeper to medical care. Again, this position could be used to induce patients to participate in research. In either case, a patient-participant could rightly claim that he or she was wronged, though not necessarily that he or she was exploited. Under Goodin’s theory, whether or not he or she was exploited would hinge on the physician-investigator’s

\[\text{Recall, for example, the Declaration of Helsinki, Article 5: “In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.” (The World Medical Association, 2004)}\]
motivations, which as described above is problematic. For example, if the physician-investigator coerced or unduly induced a patient to participate because he or she thought it was in the patient’s best interests, it would be highly paternalistic and wrongfully so. However, it would not qualify as exploitation. If however, the physician was seeking an advantage for him- or herself when he or she induced the patient to participate, the patient could rightly say that he or she was exploited.

Finally, Goodin claims that it is exploitive to play for advantage when the other party’s disadvantage stems from his or her extreme misfortune. This is consistent with the widely accepted view that it is unethical to target vulnerable populations for risky research, especially if they are unlikely to benefit from it. For instance, the Declaration of Helsinki states, “Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research” (WMA, 2004). Goodin’s theory helps give this view a theoretical underpinning by situating it in a broader theory of exploitation. Once again though, this theory is problematic in that the only guidance it provides for dealing with people who have suffered extreme misfortune is that one should not play for advantage, and that one should abide by the rules of fair play. It yields little positive guidance in the context of developing world.
Wertheimer: Exploitation as Unfair Distribution of Benefits

An Overview of the Theory

Alan Wertheimer is widely cited as an authority on exploitation, and as discussed above it seems that his theory has become quite influential in research ethics. This theory construes exploitation as a characteristic of micro-level transactions. Although to my knowledge he defines neither “micro-level” nor “transaction” explicitly, most of his examples deal with individuals. It is also clear though that larger groups can be party to a transaction. Thus, it is probably safe to assume that he had relatively small groups of individuals in mind. Wertheimer does not justify this assumption about the locus of exploitation, though he does comment on the relationship between micro-level exploitation and macro-level injustice. He concludes that they are logically distinct though they may correlate with one another: micro-level exploitation can occur in relatively just societies, but it is likely to be more prevalent in unjust societies (1996, p. 9).

Wertheimer’s project then is to separate micro-level transactions that are exploitative from ones that are not. Once again, for an interaction to be exploitative, A must (attempt) to take unfair advantage of B. But what criteria can be used to determine if A’s advantage-taking is unfair in any given case? Wertheimer considers whether

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4 Elsewhere, Wertheimer acknowledges the possibility of macro-level exploitation (2005), though to my knowledge he has not developed this.
defective consent might serve as a criterion. Defective consent, he claims, might stem from coercion or deception, but not from unfortunate background circumstances. By this definition, for example, when an economically disadvantaged person enrolls in the military because there are few other options, the consent is nonetheless valid, so long as that person understands the likely consequences of the decision and there is no threat of force (1996, p. 27). However, there are exploitative transactions that are neither coercive nor deceptive. For instance, suppose a motorist is trapped in a snow bank and a tow-truck driver offers to get him or her out for $150 when the usual rate is $50. The motorist might accept, knowing that this may be the only opportunity to be saved. Here, we would say that the tow-truck driver exploited the motorist. That is, he used his superior position to improve his own well-being unfairly. Note that the driver hasn’t coerced the motorist—that is, the tow-truck driver did not threaten to make the motorist worse off, and no reason to think the motorist was deceived. It should be noted that consent is still relevant to Wertheimer. For instance, there may be good reasons not to respect or enforce the terms of a non-consensual transaction. His point is just that defective consent is not a necessary condition for exploitation. Also note that in this example, both parties benefited, that is, if we assume that it is better to be $150 poorer than to remain stuck in the snow bank. Indeed, Wertheimer is mostly concerned with just this type of situation: consensual, mutually advantageous transactions, and how we can distinguish exploitative ones from non-exploitative ones.

5 Wertheimer accepts Nozick’s classic definition of coercion, which is restricted to situations where there is a credible threat of force (1969). Others have broader definitions.
To do so, he turns to the concept of a “social surplus.” By this he means goods that are created as a result of the transaction, that is, goods that would not exist if the transaction had not occurred. He refers to the situation in which no transaction occurred as the “no-transaction baseline.” In “mutually advantageous exploitation,” the benefits to B lie above this no-transaction baseline, but below the “fairness baseline.” To estimate where this fairness baseline lies, Wertheimer uses the “hypothetical market,” that is, he asks what the price of a given good might be in a competitive market, with many fully-informed buyers and sellers. He claims that when a seller charges more than that price because a non-competitive market allows him or her to do so, the seller has exploited the buyer (1996, p. 230). In the example given above, for example, we can say that the tow-truck driver exploited the motorist because he charged a non-market price for the service. In contrast to Sample and Goodin then, Wertheimer takes a patterned approach to the problem, placing much more emphasis on the terms of the transaction than the process that lead to them.

_A General Critique_

Wertheimer’s theory provides interesting insights into mutually advantageous exploitation. His claim that the distribution of the social surplus arising from a transaction is relevant to exploitation seems plausible. It is obviously wrong for A and B to transact and for A to get more than he or she deserves while B gets less. Moreover, I believe the wrong in this situation is correctly identified as exploitation.
However, for this theory to be workable it would require a robust mechanism for determining what is fair and the hypothetical market fails in this regard. In many cases, there is no real market for the goods or services being exchanged in a transaction. To apply Wertheimer’s theory we would have to construct a hypothetical market from scratch and this would involve making a multitude of assumptions, about supply and demand for example, to come to a standard market price. This process would be highly contentious and error-prone. In addition, even if a “hypothetical market price” could be established, there is no reason to think it would be just in any profound sense. Ultimately, Wertheimer himself retreats from claiming this. After all, the hypothetical market may exist in a profoundly unjust society in which supply and demand are set by unfair beliefs or practices. Nonetheless, he does claim that it is a non-exploitative price, or a price at which A has not taken “special advantage” of B’s vulnerabilities (1996, p. 232). Thus the hypothetical market fails to discriminate between fair and unfair outcomes of a transaction, but Wertheimer insists that the hypothetical market yields prices that are non-exploitative in the context of a given transaction.

In addition, as Sample points out, a hypothetical market approach does not correspond to our everyday use of the term exploitation. For instance, she notes that there is a competitive market for labour in the Pacific Rim. However, paying the labourers a subsistence wage while their employers earn astronomical profits is the classic example of exploitation (2003, p. 24).

Wertheimer’s use of the term also deviates from our everyday use of the term in that it limits the scope of exploitation claims to parties to a transaction. This accounts for some forms of exploitation. For instance, we might say that when a mining company pays
its workers in a poor country too little, it exploits them. However, we might also say that larger groups are exploited. For example the country as a whole could be exploited if the royalties it receives are too low, and the local community could be exploited if the operation degrades its environment. Thus, A and B might be in a non-exploitative transaction, but “C” might be adversely affected by the interaction, especially if he or she cannot intervene on his or her own behalf; the adverse effect on C should also be called exploitation.

Application to Research

Applying Wertheimer’s theory to biomedical research draws attention to the fact that research may involve potential benefits for all of the stakeholders: participants, investigators, sponsors and the general public. Thus, it could be said to generate a social surplus and is therefore a potential locus of mutually advantageous exploitation. The emphasis on the fair distribution of the social surplus seems especially important in the context of for-profit research, considering the magnitude of profits that are at stake for sponsors. It only seems fair that sponsors should share some of the benefits of research with participants, considering the critical role they play in creating this social surplus.

Wertheimer’s theory accounts for some instances of exploitation in research, such as an HIV/AIDS study conducted in Guatemala in the late 1990’s. The trial, sponsored by Merck, investigated the efficacy of twice versus thrice daily Crixivan as part of a three-

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6 Of course research can be abusive or unsuccessful, in which case some parties are left worse off.
drug cocktail and lasted for one year. Crixivan, however, is not effective alone - all three
drugs must be taken to be effective. At the end of the trial, Merck offered participants a
five-year supply of their drug, but did not provide the other two, which were
manufactured by competitors. However, the other two drugs were very expensive and
were beyond the means of the participants (Zarembo, 1999). This case is interesting in
that participants were not harmed and indeed benefitted substantially from their
participation: while they were on the trial they received effective therapy, and the sponsor
even offered them some ongoing benefits. However, it is not clear that that compensation
was sufficient, given that the sponsor’s HIV/AIDS drugs now generate over $75 M
quarterly (Merck & Co. Inc., 2007).7

Unfortunately, the hypothetical market approach cannot determine the extent of
the benefits to which participants might be entitled. Although this mechanism may have
something to contribute to the analysis of exploitation in the context of typical
commercial transactions, it seems like too much of a stretch in the context of research. To
apply this approach in research, we would have to construct a hypothetical market and
determine how it would value the contribution of participants to research. That is, we
would have to determine what benefits participants would receive if there were a large
number of fully-informed investigators and potential participants, with participants
choosing the studies that are most advantageous to them. In reality, this is rarely if ever
the case, so applying the hypothetical market approach would involve making many

7 This is the combined figure for Crixivan and Stocrin, Merck’s two HIV/AIDS drugs. Figures for
the individual drugs were not available.
assumptions that would be impossible to validate. In the absence of a better mechanism, assessing fairness would prove difficult.

Another problem with the hypothetical market is that even if it could be made to work, it yields a non-exploitative price, but not necessarily a fair price, all things considered. It is essentially conservative in that it insists that the status quo is adequate by definition and Wertheimer readily acknowledges this. This is a problem when it comes to developing world research as the healthcare that is routinely provided is often inadequate, by nearly any standard of fairness. As London writes, “the crucial problem is that [the familiar approach to international research] screens out precisely the information necessary to determine (a) whether the host community has a legitimate claim or entitlement to more than the status quo, and (b) who, if anyone, has the obligation to meet such claims” (2005).

Another weakness of Wertheimer’s theory is that it focuses on exploitation within transactions. This framing of the issue is troubling where research is concerned, though some authors have attempted to stretch Wertheimer’s theory to account for exploitation of communities in research. For example, Gbadegesin and Wendler endorse Wertheimer’s claim that exploitation relates to the benefits arising from a transaction, but try to contend that in some cases communities can be parties to a transaction as well. However, they claim that the community is only party to the transaction (i.e., research) when, “the study 1) relies on the community’s resources, including economic, social, knowledge base, or political resources; 2) focuses on the community’s customs, traditions or practices; or 3) focuses on a health feature of the community” (2006). With respect to this third point, they seem to mean a rare or unique health feature of the community, such
as an unusual genetic mutation, as opposed to a more general feature, such as a common illness that happens to be prevalent in the community. If these conditions are met, they claim, the community is truly engaged in research, and is therefore entitled to some of the benefits arising from it, taking into account its contribution relative to the other parties to the transaction.

This analysis is still overly individualistic. Although communities can seemingly be exploited *qua* communities under the conditions the authors describe, one might also say that communities can also be exploited when their members are exploited. Even if one goes along with Wertheimer’s claim that exploitation occurs when the exploitee receives less than his or her fair share of a transaction’s “social surplus,” there are still implications for the community. The individuals in question are part of a web of social relationships and if they are exploited, they will have less to offer to the community. For example, if we assume that some placebo-controlled trials are exploitative, the immediate effects of being assigned to the placebo arm are borne by the individual. However, there are indirect effects on others, such as the participant’s friends and family, who have to deal with the fact that their loved one is less healthy than he or she would have been if he or she was in the active arm of the trial, or if the trial had used an active-control design in the first place. In this sense, the community is exploited when the individual is exploited. However, Wertheimer’s theory and Gbadesin and Wendler’s application of it discount this possibility as they assume that persons are first and foremost individuals. This is not unique to them, nor is it a new phenomenon; 20 years ago Levine wrote that,

> In each of its publications, it [the National Commission] seems to embrace an atomistic view of the person. The person is seen as a highly
individualistic bearer of duties and rights; among his or her rights, some of the most important are to be left alone, not to be harmed, and to be treated with fairness. Except, perhaps, in its report on research involving children, there is little or no reference to persons in relationship to others or as members of communities. (1988, p. 13)

A more communitarian approach would give greater weight to such relationships. As Charles Weijer comments, “The communitarians argue that the principle of respect for persons must take account of the fact that an individual is situated within a particular community” (1999). It is especially important to understand that people are members of communities where health is concerned. Charlene Galarneau offers four reasons why this is so: firstly, our understanding of the meaning of health and disease is conditioned by the communities in which we live; secondly, communities have an impact on our health; thirdly, healthcare involves multiple community-based relationships; and fourthly, communities as a whole, and not just individuals, benefit from healthcare. Based on this, she argues that just resource allocation in healthcare has an important community dimension (2002).

Subsequent sections of this thesis will explore the relationship between the individual, his or her community and exploitation. Under Sample’s theory, described below, both individuals and communities can be the object of exploitation claims. Chapter Three will consider research that is not responsive to community health priorities, arguing that according to Sample, such research exploits both the individual participant and the community in which it is conducted. My point here is that a Wertheimerian analysis cannot accommodate this possibility.
Sample: Exploitation as Degradation

An Overview of the Theory

Whereas Goodin construes exploitation as a particular kind of failure to protect the vulnerable, Sample’s theory views it as a lack of respect for persons, and more broadly respect for other beings. (She argues convincingly that entities such as animals and ecosystems can also be exploited in the morally charged sense.) The crux of her theory is the following:

The basic idea is that exploitation involves interacting with another being for the sake of advantage in a way that degrades or fails to respect the inherent value in that being. It is this lack of respect that explains the badness of exploitation. The consequences of such disrespect are connected to, but not constitutive of, the exploitation. (Sample, 2003, p. 57)

Sample has a complex notion of respect and she explains it at some length. Briefly, she begins by noting that respect for something entails accepting that there are limits on the way one may interact with it. In her thinking, the notion of respect is closely tied to that of “engaging with value.” She draws extensively on Joseph Raz’s Value, Respect and Attachment, which asserts that such engagement comes in three stages: firstly, acknowledging in thought and in speech that the thing has value; secondly, taking steps to preserve it; and thirdly, interacting with it in meaningful and appropriate ways.
Respect for something, however, only entails the first two (Raz, 2001, pp. 161-165). For example, in order to respect a work of art, one need only psychologically accept that it is valuable and take steps to avoid destroying it. One need not become a connoisseur of art in order to respect it.

Moreover, Raz argues that “the duty of respect is not a duty to seek out, identify and engage with whatever has value. Rather, it is a duty to acknowledge, to refrain from harming, and to some degree to preserve what valuable things we do encounter” (2001, p. 68). It would clearly be impossible to seek out, identify and engage with everything that has value. By limiting the duty of respect to “things we do encounter,” he provides a plausible basis for Sample’s claim that exploitation occurs in interactions and relationships, but not between people who have no connection to each other. Understood this way, the duty of respect may account for the idea that in a transaction or relationship one may have an obligation to improve the other party’s situation, even though we may not recognize such an obligation towards strangers.

She claims that a lack of respect falls into one of three categories: firstly, neglecting what is necessary for that person’s well-being or flourishing; secondly, taking advantage of an injustice done to the person; and thirdly commodifying an aspect of the person that should not be commodified. With respect to what is necessary for a person’s well-being or flourishing, Sample rejects Rawls’ account, which revolves around the notion of “primary goods.” Instead, she invokes Martha Nussbaum’s “capabilities approach,” which holds that a just society will ensure that even its worst-off members have a certain baseline of capabilities, such as the ability to enjoy bodily integrity, senses, imagination and thought (2003, p. 78). With respect to taking advantage of previous
injustices, Sample argues that to do so also fails to treat people with the respect they deserve. For example, she notes that in the past, it was possible for White Americans to pay Black people less than they deserve because of the history of slavery and discrimination in the U.S. Sample would argue that such low wages are exploitative even though they may be the standard rate of pay. This differs from Wertheimer’s theory in that he claims that exploitation can only take place at non-market prices and I believe this is a major advantage of Sample’s theory over Wertheimer’s. Finally, with respect to commodification Sample rightly points out that our core notion of exploitation includes the idea that, “using a vulnerability in order to force certain things into a market is exploitative and wrong” (p. 83). However, she is admittedly agnostic on what aspects of a person should not be commodified.

It should be noted that Sample’s understanding of “interaction” appears quite broad. It is not limited to face-to-face interactions, but includes commercial transactions where the parties are oceans away from each other. Moreover, her interactors can be individuals, but also countries, and she devotes a whole chapter to the question of whether globalization is inherently exploitative (2003 p. 131-171). In such a broad framework, it is possible that two parties are “interacting” without knowing that they are doing so, as in the sweatshop labourer and the Western consumer.

Finally, the concept of vulnerability plays a role in Exploitation as Degradation. Sample takes the middle ground between Goodin, whose entire theory is dependent on vulnerability and Wertheimer, who discounts vulnerability as an incidental feature of some exploitive transactions. She writes that, “Exploitation as Degradation is connected to vulnerability because vulnerability is typically (if not always) at the root of
exploitation. When we exploit others, we make use of their genuine need for the sake of advantage in ways that fail to respect them” (2003, p. 75; emphasis added).

A General Critique

Overall, I believe that Sample’s theory is the best account of exploitation of the three. It is consistent with our everyday understanding of exploitation while providing a rigorous account of its philosophical underpinnings. Sample argues convincingly that her theory satisfies the conditions described above:

the requirement of an ethically thick interpretation of the concept… is consistent with a moderate view regarding the demandingness of moral obligations, explains why we regard exploitation as worse than neglect, and [allows us to] talk meaningfully about exploitative systems in addition to exploitative transactions. (2003, p. 59)

There are at least three theoretical weaknesses to Exploitation as Degradation though. Firstly, as Jeremy Snyder points out, not everyone shares Sample’s intuition that exploitation is worse than neglect. He writes, “opponents can reasonably hold that it cannot be worse to benefit another, albeit inadequately, than to stand by and allow the suffering to occur” (2006, p. 119). Essentially, he is pointing out that Sample is a deontologist and not a consequentialist, and she is quite forthright about this.

Secondly, Wertheimer provides a similar, but distinct criticism. He writes, “Is degradation a function of the way in which A treats B or the effect of A’s treatment of B on B?” (2007, p. 259) This, criticism also reduces to whether exploitation should be
understood in deontological or consequentialist terms, though his approach is slightly
different. He takes the example of a person, A, who hires a prostitute, B. If we assume
that a person’s sexuality should not be commodified, then we might say that A exploited
B in the transaction. However, if B regards him- or herself as a professional and doesn’t
feel exploited by the transaction, in Wertheimer’s view, it is unclear that there is anything
wrong with it. This example is interesting because it highlights the fact that Sample has
not considered the situation in which the parties have different values. It is not clear
whether she would find the situation described above exploitative.

Thirdly, Sample claims that there are three categories of lack of respect, as
discussed above. This limitation seems unjustified. For example, to insult someone is to
disrespect him or her, even though this does not fit neatly into one of her three categories.
She also rejects Wertheimer’s notion that paying less than the market price for something
is exploitive. I disagree: it seems to me that paying someone less than they deserve is
often an instance of “failing to respect their inherent value.” As Snyder writes, “Sample
should allow that Wertheimer identifies a form of exploitation, while maintaining that her
120)

Application to Research

Just as I believe that Sample’s account of exploitation is the strongest
theoretically, I believe it provides the richest analysis of exploitation in the context of
research. Although, I have no major objections to the theory, there are two areas where further development would be needed to apply the theory to research.

Firstly, one of the limits of Sample’s theory, which she readily acknowledges, is that she remains agnostic with respect to what aspects of a person should be subject to the market. It is not clear then how she might view research participation, particularly participation in studies that support the development of a commercial product. Clearly, there is the potential for commodification here. For instance, Tishler and Bartholomae describe a group of “professional guinea pigs,” that is, healthy volunteers who repeatedly enrol in clinical trials, presumably motivated by financial compensation (2003). Should their healthy bodies be the object of a commercial transaction? Similarly, some research on sick patient-participants could be said to commodify their bodies as well, even though this research seldom offers participants cash payments. It is evident from some accounts that pharmaceutical companies and especially contract research organizations regard such participants as scarce resources that can be used to generate a profit (Petryna, 2006). Is this inappropriate commodification? To answer these questions would require further theoretical work.

Secondly, Sample claims that transactions that neglect the weaker party’s flourishing and well-being are exploitative, specifying that a capabilities approach would be the appropriate measure to use here. In addition, she acknowledges that “[non-exploitative interaction] does not necessarily entail an obligation to provide our interactors whatever they need in order to flourish” (2003, p. 81). However, she doesn’t provide a mechanism for determining the extent of one’s obligations to one’s interactors.
Presumably such a mechanism would account for the nature and extent of the relationships.

A major advantage of Sample’s theory over Wertheimer’s is that it does not restrict itself to micro-level transactions; indeed she suggests that it might be applicable to animals and ecosystems. It follows that communities of human beings can be the object of an exploitation claim, even if they are not, strictly speaking, a party to any transaction. This allows us to criticize certain research studies which would be unobjectionable in a Wertheimerian paradigm. For instance, some research that is unrepresentative of local health priorities might fall into this category; we might say that this research exploits the community because it is not sufficiently attentive to its well-being and flourishing. This argument holds even if the individual participants are not exploited. An example might be the “Milan ADA-SCID Study,” (Aiuti, et al., 2002) in which two children from developing countries were recruited for a highly experimental gene-transfer treatment for ADA-SCID. Kimmelman has provided a thorough analysis of the conduct and ethicality of the trial (2007). What matters here is that the study (arguably) offered the participants fair benefits, so the trial cannot be criticized on a Wertheimerian account. However, the study was examining a condition that was not a major concern in Palestine and Colombia, where the participants were recruited, at least not from a public health point of view, and the intervention if ultimately proven effective, probably wouldn’t be made available in those countries. On Sample’s account, there are ample grounds to criticize the study: there are pressing public health concerns in those countries and the Milan Study obviously wasn’t designed to address them. This might qualify as “insufficiently attentive to the well-being and flourishing” of the communities.
Additional Comments on Exploitation and Developing World Research

Before concluding this discussion of exploitation in developing world research, I would like to draw attention to two more pertinent issues. Firstly, it should be noted that there is always uncertainty with respect to the outcome in research. For sponsors, this means that their novel product may be inferior to existing treatments or no better than placebo. Thus, the considerable funds invested in a trial may be lost, though it should also be noted that sponsors can spread their risks over several trials on several products. On average, drug development is highly profitable. Participants also face risks, though the stakes are much higher for them: their health and survival may be at risk. Indeed, they may be forced to gamble if the study does not meet the highest ethical standards in that there may be an unduly high risk of adverse events from investigational treatments and experimental procedures and they may be randomized to a placebo. Thus, to use Ballantyne’s terminology, they may be forced to gamble “with and for basic goods” (2005). She argues that this is fundamentally unfair.

The basic goods are considered to be the grounds upon which one builds a fruitful and fulfilling life. As such they should be guaranteed to the greatest extent possible to all people. This first principle of fairness therefore deems as unfair situations in which individuals denied basic goods as a result of global social structures are left to undertake risky gambles with what they have in order to try and achieve the basic goods they lack. (2005, p. 480)
The incommensurate nature of the risks faced by sponsors and participants has at least two implications for the analysis of exploitation in research. Firstly, some theorists argue that if A tries but fails to derive an unfair benefit from his or her interaction with B, it should not be regarded as exploitation. This seems out of place in the context of an “unsuccessful” clinical trial; the unfair treatment of participants in such research is still exploitative. Secondly, the serious risks faced by participants suggest that it is unfair for their fate to depend on their randomization to one arm of a trial. If the trial is not in clinical equipoise (which would be problematic in itself) the less favourable arm should be the basis of any judgment on the fairness of the benefits.

A second issue that needs further attention is the connection between vulnerability and the validity of consent. When research is conducted in the developed world, one of the main things participants must understand is what they are giving up by participating in research. For instance, they may be giving up the opportunity to have their physician tailor their treatment regimen to their individual needs. However, in the developing world, participants may not be giving up anything by participating in research. In fact, it may be the lack of other options that motivated them to participate in the first place. A Nigerian researcher is quoted as saying,

Because of the scarcity of everything, to be talking about a choice [is questionable]. . . in the US you can ask questions, you can ask for a second opinion, but that doesn’t happen here. We are challenged . . . by poverty by lack of literacy, by education of what basic rights a person has. [The] power [of these factors] is too awesome. (Lavery, Grady, Wahl, & Emanuel, 2007, p. 321)
This has important implications for the meaning of informed consent, which ordinarily serves two purposes. At a minimum, consent must be voluntary and uncoerced; these are Wertheimer’s requirements for the validity of consent. In research, insisting that potential participants decide for themselves whether or not to enrol and not allowing authorities to decide for them ensures that they are not abused. However, it also serves another purpose: giving potential participants ample information allows them to choose the course of action that is most closely aligned with their considered life-plans. That is, it promotes autonomy and respect for persons. However, when participating in a study is the only viable option, consent may be voluntary and uncoerced, but not fully autonomous. That is, potential participants may not be under any threat to enrol and they may fully understand the consequences of doing so but if their basic needs are not met, the notion of making choices that are aligned with their life-plans is meaningless (Zion, 2005). That is not to say the research is unethical because the consent was not given under ideal circumstances. Rather, one should be particularly mindful of the fact that this particular form of vulnerability has lead participants to enrol.
Conclusion

This chapter has critically assessed several theories of exploitation as they relate to biomedical research. It examined Robert Goodin’s “Exploitation as Vulnerability,” as a point of comparison for Wertheimer and Sample’s theories. However, I will draw most extensively on Wertheimer and Sample’s work in the remainder of this thesis. I have shown that Wertheimer’s theory cannot account for all instances of exploitation in research or in other contexts. By focusing on transactions, it neglects the possibility groups who are not parties to a transaction can be exploited and limits the scope of exploitation claims to individuals or relatively small groups. Moreover, by insisting that the distribution of the social surplus is the only relevant concern, it screens out many potential instances of exploitation. Sample’s theory is much broader in scope. It allows for exploitation of both individuals and communities, has more tenable criteria for exploitativeness and comes closer to everyday use of the term.

This chapter has distinguished between several theories of exploitation and argued that Sample’s is superior. Although this is debatable, the fact remains that there are several distinct conceptions of exploitation. For the sake of clarity (and at the expense of linguistic comfort) I will refer to them as Wertheimerian exploitation and Samplian exploitation.
CHAPTER THREE: EXPLOITATION AND CODES OF ETHICS

Introduction

Many laws, regulations and guidelines define the ethical conduct of research. Because the exploitation of research participants is a central concern, one of these policies’ main purposes is to provide guidance on avoiding it. For instance, Emanuel, Wendler and Grady write: “Ethical requirements for clinical research aim to minimize the possibility of exploitation by ensuring that research subjects are not merely used but are treated with respect while they contribute to the social good” (2000, p. 2702).

In some cases, the intent to avoid exploitation is explicit. For instance, the framers of the CIOMS Guideline write that, “The challenge was to encourage research for local solutions to the burden of disease in much of the world, while providing clear guidance on protecting against exploitation of vulnerable communities and individuals” (CIOMS, 2002). Similarly, the TCPS notes that the principle of justice entails not exploiting vulnerable individuals: “[Distributive Justice] thus imposes particular obligations toward individuals who are vulnerable and unable to protect their interests to ensure that they are not exploited for the advancement of knowledge” (Medical Research Council of Canada et al, 2003). Others do not specifically mention “exploitation,” but there is nonetheless reason to think that they were promulgated to prevent it. For example, the U.S. Common Rule was promulgated in response to the Belmont Report which describes the treatment of prisoners in Nazi concentration camps as exploitative (The National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research, 1979), and
suggests that the Tuskegee study was too. In other cases, there is no reason to think that the purpose is to avoid exploitation, except the text itself. It should also be noted that these guidelines serve many other purposes, for example, to prevent outright abuse, to prevent deception, even where this is not exploitative and to describe procedural requirements for record keeping. Nonetheless, preventing exploitation remains an overarching concern.

These policies differ from one another in two important ways. Firstly, they vary in their particular requirements and their overall stringency. For instance, some permit a wide range of placebo-controlled trials while others set very strict conditions on placebo use. Likewise some adopt a lowest-common-denominator approach, offering few substantive rules while others articulate high ethical standards to which investigators should aspire. These differences suggest that the promulgators of the respective policies have different views of what is owed to research participants by way of non-exploitation. Secondly, the policies vary in legal force: some have the full force of law, while others have no legal force, but remain influential as moral guidance. In this chapter, I will examine several such policies. In decreasing order of legal force, they are: the U.S. “Common Rule,” the ICH-GCP Guideline, Canada’s Tri-Council Policy Statement, the Declaration of Helsinki, the CIOMS Guideline and the UNAIDS Guideline. Clearly these six represent only a small fraction of the hundreds of policies that guide the conduct of research in various jurisdictions (OHRP, 2008). Nonetheless, I believe that they are among the most influential in international research, and they represent a wide range of approaches to governing the conduct of research. This chapter will also briefly consider two influential reports on the topic: NBAC’s Ethical and Policy Issues in International
Research: Clinical Trials in Developing Countries (2001) and the Nuffield Council’s The Ethics of Research Related to Healthcare in Developing Countries (2002), as well as research ethics policies from two developing countries: South Africa and India.

In order to focus the analysis, this chapter will be limited in two ways. Firstly, it will not consider “special populations,” for example, children, institutionalized individuals and adults who are unable to consent for themselves, nor will it discuss the inclusion of women in research, or gender as an important consideration in justice and research. Secondly, it will focus on some of the more controversial provisions of some policies, namely post-trial access to treatment, the use of placebos and responsiveness to local health needs. I will argue that these provisions are more closely aligned with Sample’s thinking. These provisions, however, tend to appear only in the more “aspirational” policies; those that have more legal force tend to take a more Wertheimerian approach.

This chapter will expand on the work of Lavery, who has made similar observations. Relying heavily on Wertheimer for his understanding of the theoretical underpinnings of exploitation, he notes that

In the United States, these rules are codified into federal regulations that must be followed by institutions and investigators to ensure their eligibility to receive public funding for their research activities. In contrast, international guidelines such as the Declaration of Helsinki, the CIOMS Guidelines, and the UNAIDS Ethical Considerations are not legally binding documents” (2004, p. 324).
It will analyze these policies in greater detail and add the ICH GCP Guideline and the TCPS.

**Framing the Issue**

As discussed in Chapter Two, Wertheimer views exploitation as a characteristic of some *transactions*; Sample views it as a characteristic of some *interactions*. The difference in their terminology seems subtle, but it is actually quite significant. A transaction is the exchange of goods or services between parties and the terms thereof; an interaction is something much broader, including the entirety of how people behave towards each other. This section will argue that research ethics policies view research participation more as a transaction than an interaction.

These policies require that research be described in a protocol and submitted to an REC for approval. RECs are required to judge, based on this document, whether the risks of a particular study are reasonable in proportion to the benefits. Some policies instruct RECs to use “component analysis” (Weijer, 2004) for this assessment. Under component analysis, the risks of therapeutic components of a study are weighed against their therapeutic benefits to the patient; the risks of non-therapeutic procedures are weighed against the value of the knowledge that stands to be gained from them.

While there are good reasons for describing research in a protocol and for RECs to conduct a risk-benefit analysis, these procedures encourage RECs and investigators to assume that the protocol completely describes all ethically relevant aspects of the conduct of the study. In reality though, each potential participant is a unique individual and
participating in the study means something different to each one. Even if a study appears ethical on paper, there may be reasons why a particular participant should not enrol. For instance, if financial compensation is offered for participating in a study, the REC must decide the amount and the terms under which it is paid out. Although they might find the terms reasonable, from the point of view of an impoverished participant, it might seem like a very large sum. He or she might enrol in the study for the money, and not out of altruism or because the investigational treatment is in his or her best interests. However, the REC does not have access to this “background information” in the protocol.

Similarly, Kimmelman writes that “the risk assessment process used in trial oversight addresses risks selectively and may not respond to risk in a manner consistent with the priorities of many trial participants” (2004).

Thus, the documents submitted to RECs describe research more a transaction than an interaction. By judging the study on the basis of these documents, RECs may be tacitly promoting the idea that research participation is a transaction, as opposed to an interaction. In this respect, the approach of many ethics policies is more closely aligned with Wertheimer.
Placebos, Representativeness and Post-Trial Benefits

The previous section argued that in one respect many research ethics policies are Wertheimerian, but in others, they are more Samplian. These Samplian requirements include some of the more controversial articles of the Declaration of Helsinki, namely article 19, which deals with fair selection of participants, article 29, which deals with placebo control groups, and article 30, which deals with post-trial access to medications. Although the Declaration of Helsinki has generated the most discussion, the policies discussed here all deal with these some of topics to some degree. In this section, I will consider these issues one by one, showing the range of positions taken by the different policies, and applying Samplian and Wertheimerian analyses to each. I will draw particular attention to their implications for individual research participants and for broader communities. Then, I will provide a summary of where each policy stands on each issue.

Fair Selection of Participants and Responsiveness

In the context of research, distributive justice refers to fairness in the distribution of harms and benefits associated with participation. However, there are differing opinions on the extent of the obligations that stem from distributive justice. The base requirement seems to be that especially vulnerable individuals should not be used for risky research merely because they are administratively convenient. Historically, for example, healthy prisoners were used extensively for early phase drug development (Hornblum, 1998); this
represents an obviously unfair distribution of benefits and burdens, and clearly represents an instance of Wertheimerian exploitation. In other words, it constitutes a transaction in which B (the prisoner) receives an unfairly low level of benefits (and indeed they were outright harmed) in return for their interaction with A (society at large and the investigators acting on its behalf). This was possible because the prisoners were exposed “non-market conditions,” that is, they only participated in the transaction because of their limited freedom. Obviously, individuals who were not imprisoned would not have accepted to have this research conducted on them. This research would also be problematic for Sample, for all three of her reasons.

A next step in selecting subjects fairly is ensuring that research is not conducted in populations that are unlikely to benefit from it. The Declaration of Helsinki states this principle most succinctly: “Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research” (WMA, 2004). This goes beyond the first step, in that it suggests that units larger than the individual are relevant to the ethics of research. However, it is still a negative obligation— it instructs researchers not to do certain research unless certain conditions are met. Despite this policy, non-responsiveness is a central problem in developing world clinical trials. These settings may offer ideal conditions for testing new products, but these products may be so expensive that they are not accessible to the local population. Such research would not constitute Wertheimerian exploitation. According to Wertheimer, as long as the individual is compensated adequately, there is no need to consider larger groups of people. However, Sample’s more holistic vision of exploitation might include such research if it indeed takes advantage of past injustices.
Moreover, it could be said that it is not sufficiently attentive to what is necessary for the individual’s flourishing and well-being, namely being part of a community. As discussed above, exposing oneself to research risk would ideally be altruistic. However, when the benefits of research flow to individuals with whom the participant feels little connection, such as wealthy people in distant countries, and do not flow to one’s own community, it could be said to betray the participant’s capacity as a community member.

Another issue related to fair subject selection is engagement with local populations. This goes a step beyond the previous requirement in that it creates a positive responsibility, namely to do research that is relevant to their health needs, and not merely a negative obligation, that is, an obligation not to do research whose fruits will not be made reasonably available to the population in which it was conducted. Emanuel, Wendler and Grady do not mention the responsiveness requirement in their 2000 article. There, they treat knowledge and “social value” as benefits that are homogenously distributed over all of society. However, their subsequent article “What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research” acknowledges the importance of determining who the beneficiaries of research are likely to be and the need for collaborative partnerships with local populations to ensure that research is responsive to their needs (Emanuel, Wendler, Killen, & Grady, 2004).

Engagement goes beyond both Wertheimer and Sample who are mainly concerned with the negative obligation not to exploit. Recall that Sample’s notion of respect has three stages: appreciating the object of respect, avoiding harming it and engaging with it in meaningful ways; failure to appreciate or avoid harming it constitutes exploitation. However, she does not argue towards an obligation of engagement. Such an
obligation, however, may be rooted in Rawlsian conceptions of justice, as discussed in Chapter Five.

Control Groups

The use of placebo controls in developing world research remains one of the most hotly contested issues in the field. Indeed it was placebo-controlled trials of AZT to prevent mother-to-child transmission (MTCT) of HIV that first drew attention to the ethics of research in the developing world and prompted the controversial revision of the Declaration of Helsinki in 2000. The chief criticism of the MTCT trials was that children of the participants in the control group might have been saved from HIV infection had their mothers received an active comparator. These studies were ethically questionable because the comparator arms were arguably not in clinical equipoise.⁸

As with fair selection of participants, there is a range of positions on when placebo-controlled trials are acceptable. Some policies permit a wide range of placebo-controlled trials. The ICH, for example, has an entire document devoted to the choice of control groups (ICH, 2000), though its position is relatively weak. As mentioned above, it concludes that the acceptability of a placebo control is ultimately up to the judgement of

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⁸ Although there are various formulations of the principle, Freedman’s holds that it is only ethical to enroll a patient in a randomized trial if there is “present or imminent controversy in the clinical community over the preferred treatment,” and that the study must be designed to settle that controversy (1987).
the investigator, REC and the patient. The CIOMS guideline lies at the other end of the spectrum - it only allows inactive controls in a narrow range of situations. It states:

Placebo may be used: when there is no established effective intervention;
when withholding an established effective intervention would expose
subjects to, at most, temporary discomfort or delay in relief of symptoms;
when use of an established effective intervention as comparator would not
yield scientifically reliable results and use of placebo would not add any
risk of serious or irreversible harm to the subjects. (2002, emphasis added)

Thus the CIOMS guideline comes close to endorsing clinical equipoise, but
allows deviation from it when the consequences of using a placebo-controlled design are
relatively minor. It is difficult though to ground the principle of equipoise in
Wertheimerian exploitation. Again, Wertheimer focuses on what benefits the individual
receives as a result of participating in a transaction. If we consider a trial that is not in
clinical equipoise, for example because some participants are randomized to placebo
when effective therapies are known to exist, Wertheimer might ask whether the benefits
to the individual randomized to placebo are fair. (If this is the case, the benefits to a
participant receiving active treatment would presumably be greater, and therefore more
than fair.) As discussed in Chapter Two, it is difficult if not impossible to apply a
hypothetical market to research participation. However, such an approach would not

9 Under some economic models, Wertheimer would ask whether a 50/50 chance of receiving
active drug is fair. However, I believe that in this context, it is more appropriate to judge the transaction
based on what a participant randomized to placebo would receive. This is discussed above under
“Additional Comments on Exploitation and Developing World Research.”
consider a person’s entitlement to standard care. To Wertheimer, the fact that an individual is arbitrarily assigned to a less-than-optimal therapy is irrelevant; as long as he or she receives an adequate share of the social surplus, the transaction is non-exploitative.

In contrast, Sample gives us ample grounds to criticize trials that are not in clinical equipoise. Randomizing an individual in a study with a placebo arm could be degrading in itself, especially if that individual is compelled to participate because of past injustices and if the research as a whole is not sufficiently attentive to his or her well-being. Similarly, trials that are not in equipoise could be degrading to the community if its members degraded. Such a trial would also be especially disrespectful to the community if it is not responsive to local health needs.

Post-Trial Benefits

Researchers’ responsibilities to research participants at the end of a clinical trial are another area in which Wertheimer and Sample might come to very different conclusions. Concerns about post-trial obligations are especially grave in research on conditions that require ongoing treatment, such as HIV. In the worst case scenario, participants are given effective life-sustaining therapy while on a trial but then cut off as soon as the research ends.

Once again, research ethics policies take a wide range of positions on this issue. For example, the ICH-GCP guideline has no provision at all for post-trial benefits (1996). At the other end of the spectrum, the 2000 revision of the Declaration of Helsinki specifies that, “At the conclusion of the study, every patient entered into the study should
be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study” (World Medical Association, 2004). However, the footnote added in 2004 weakens this requirement, stating that concerned parties must negotiate arrangements for post-trial access at the beginning of research. Prior negotiations are also mandated by the CIOMS Guideline and the UNAIDS Guideline.

Some commentators have already applied a Wertheimerian analysis to the issue of post-trial access. Drawing directly on Wertheimer’s conception of exploitation, they argue that a “fair benefits” standard should be applied to research. They claim that the “reasonable availability” standard is not a reliable mechanism for determining what research participants are ethically entitled to as it is only applicable to late-phase clinical trials and that in some cases it imposes an unduly heavy burden on research sponsors, while in others it gives participants less than they deserve. Instead, they claim that participants and their communities should receive “fair benefits,” which might or might not come in the form of access to an intervention. Echoing Wertheimer, they write, “Exploitation is about “how much, not what, each party receives. The key issue is fairness in the level of benefits” (The Participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries, 2004, p. 19).

These critics are correct in pointing out that the “reasonable availability” requirement is flawed in that it does not seem applicable to all types of research. However, they dismiss it based on Wertheimer’s concept of exploitation without taking Sample’s into account. From Sample’s point of view, providing participants with ongoing benefits is not just a matter of compensating them fairly for their contribution to the research. It is about treating participants with respect: providing them with the
medications they need is the perfect example of being attentive to their flourishing and well-being. On this issue, NBAC comments that, “making the benefit responsive to the health needs of the participants provides an additional way to ensure that research participants are not exploited” (NBAC, 2001, p. 60). It is much more direct and meaningful way of engaging with participants and their communities than some of the measures that the authors propose such as long-term research collaboration and profit-sharing agreements.

A Comparison of the Policies and their Legal Force

The preceding section provided brief Wertheimerian and Samplian analyses of different issues in research ethics; these are summarized in Appendix I. In this section, I will discuss where the policies in question stand on these issues. I believe the issues in question are key indicators of the policies conception of exploitation and suggest whether they are more Samplian or Wertheimerian in orientation.

The U.S. Common Rule

The U.S. Common Rule (formally the Code of Federal Regulations Title 45: Public Welfare Part 46: Protection of Human Subjects) is the earliest of the policies discussed here. Unlike the others it is part of the Code of Federal Regulations is considered formal administrative law in the United States. Promulgated by the
Department of Health and Human Services, it sets the standard to which research funded by the American granting agencies must adhere. Moreover, a precedent established by Chevron U.S.A., Inc. v. Natural Resources Defence Council, Inc., 467 U.S. 837 (1984) reinforces executive departments’ authority to interpret statutes for which they are responsible. Thus, it has far more legal force than any of the other policies considered here.

However, the Common Rule is thick on procedure and thin on substance. With the exception of research on special populations such as prisoners and pregnant women, the substantive guidance is found mostly in subsection 111, “Criteria for IRB approval of research.” Briefly, the rules in this section pertain to minimizing risk, ensuring that research risks are reasonable in proportion to benefits, ensuring that subject selection is equitable, determining whether procedures to obtain and document informed consent are adequate and guaranteeing subject safety and privacy, as well as ensuring that vulnerable subjects are adequately protected. Subsequent sections explain the informed consent requirements in greater detail. With respect to the selection of participants, it states, “Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted...” (2005) Although this is somewhat vague, it seems to stop short of requiring that research be responsive to the needs of the populations in which it is conducted. It is silent on the issues of control groups and post-trial obligations to participants. Overall the Common Rule is focused very much on protection of the individual research participants

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10 It does not distinguish between therapeutic and non-therapeutic risks.
during the course of research and it has none of the provisions that I have identified as being aligned with Sample.

The ICH GCP Guideline

The ICH GCP guideline differs substantially from the other policies mentioned here in that its main purpose is to harmonize the requirements for submission of clinical trial data in the three ICH regions; it is not primarily an ethics guideline. The ICH website notes that, “The purpose is to make recommendations on ways to achieve greater harmonisation in the interpretation and application of technical guidelines and requirements for product registration” (2008). Nonetheless, this guideline provides some standards with respect to the ethical conduct of research, hence its inclusion here. Its importance should not be understated though. The ICH GCP guideline was negotiated by the regulatory authorities of Europe, Japan and the United States; other countries (such as Canada) have observer status. Compliance is mandatory for studies used to support applications to market drugs and biologics in the world’s three largest markets for pharmaceuticals. Therefore, even though it is not considered to be a formal instrument of international law, it is highly influential where pharmaceuticals are concerned. In addition, the laws and regulations of various countries (including Canada) make references to internationally accepted standards of good clinical practice or similar statements (Food and Drug Regulations, 2009, C.05.010), which are generally understood to include the ICH GCP guideline, among others.
Although the ICH GCP Guideline offers extensive procedural guidance, particularly with regards to data integrity and the responsibilities of various parties involved in the conduct of research, it has very little substantive guidance on the ethical conduct of research. For instance, section 3.1 deals with the responsibilities of IRB/IECs: these include safeguarding the rights, safety and well-being of all trial subjects and reviewing various documents associated with the study. However, it provides few substantive rules on how to judge whether participants’ rights, safety and well-being are adequately safeguarded, except to repeatedly refer to “applicable regulatory requirements.” The ICH GCP Guideline does not deal with the fair selection of research participants except to note (in article 3.1.6) that non-therapeutic research on participants who are unable to consent for themselves may raise ethical concerns that the REC should address. As previously discussed, the ICH’s Guideline E10 deals with the choice of control group in clinical trials and it does not endorse clinical equipoise as a requirement for ethical research. Once again, it concludes that the acceptability of a placebo-controlled trial should be judged on a case-by-case basis by investigators, RECs and patients. This process may not create a problem in developed countries, where other regulations set the bar higher than ICH, and where patients would be relatively unlikely to enrol in a study with a sub-optimal comparator. However, it is highly problematic in areas where any additional regulatory requirements are overly lax or where people do not have viable options outside of research. Finally, the ICH GCP Guideline does not speak to post-trial benefits for participants or their communities.

It should be noted that the Guideline does appear to endorse the declaration of Helsinki. Article 2.1 reads, “Clinical trials should be conducted in accordance with the
ethical principles that have their origin in the Declaration of Helsinki...” This, however, is misleading. The Declaration is a “living document” (as evidenced by its many revisions) that evolves over time to reflect new thinking in research ethics and the WMA on its website, insists that only the current version has its endorsement. However, clinical trial protocols often refer to the 1989 version of the Declaration. Thus, they technically meet the ICH’s requirement but avoid having to comply with the stringent requirements imposed by the 1996 and 2000 revisions.

Like the Common Rule, the ICH GCP guideline focuses on the well-being of research participants during the course of research and contains none of the provisions that I have identified as particularly Samplian.

*The Tri-Council Policy Statement*

The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS) is Canada’s main guideline for the ethical conduct of research (Glass & Lemmens, 2002, p. 477). It is promulgated by the country’s three federal granting agencies and in order to obtain funding from them, investigators and institutions must comply with it. Therefore, it applies not only to research funded by these agencies, but to all research conducted at the country’s major academic institutions and their affiliated hospitals, as well as research conducted by their faculty, even while they are abroad. In fact, it is explicit on this last point, stating that, “An institution is responsible for the ethical conduct of research undertaken by its faculty, staff and students regardless of the location where the research is conducted” (Medical Research Council of Canada et al.,
2005, p. 1.12). However, as Glass and Lemmens note, research conducted with private funds outside of these institutions and by individuals not affiliated with them is exempt (2002, p. 477).

The TCPS requires that institutions receiving CIHR funds “certify that they comply with this Policy regarding research involving human subjects” (p. i.2). However, neither the policy itself nor the agencies that endorse it have an active mechanism for ensuring compliance. According to the CIHR website, for example, “CIHR does not have a regulatory or a quasi-judicial mandate. CIHR does not investigate allegations of non-compliance with research policies. CIHR refers allegations to the institutions for investigation and requires the institutions to report back their findings” (CIHR, 2007). It does, however, impose sanctions for violations where institutional disciplinary measures would be insufficient, and although it has done so in academic integrity cases, it has never done so for violations involving the rights and well-being of human research subjects (CIHR, 2007).

The TCPS, in my opinion, provides protections to clinical trial participants that are somewhat more rigorous than the preceding two policies, though it is currently under revision and its provisions may be strengthened or diluted as a result. Still, the current version endorses equipoise and component analysis, separating therapeutic from non-therapeutic procedures (2005, p. 1.5 and 7.2). Moreover, it prohibits placebo-controlled trials that are not in clinical equipoise except in cases where the condition being treated is relatively minor (2005, Art. 7.4). It also contains some guidance on justice and research, noting that vulnerable individuals should not be targetted for risky research (2005, p. i.6), though it stops short of requiring that research be representative of the needs of the
populations in which it is conducted. Although it notes that “Canadian society legitimately expects that the benefits and harms of research shall be fairly distributed,” (2005, p. i.2) it does not impose obligations on any party to make this so. Finally, it is especially vague with regards to post-trial benefits. In typically irresolute language, it states:

Researchers should ensure that the benefits of their research are available in the host country. Benefits may, for example, take the form of information-sharing, training for local personnel both in the host country and in Canada, or health care or similar services. However, since researchers are not aid agencies, REBs should not try to force them to undertake aid work. (Medical Research Council of Canada, 2005, p. 1.12)

This passage is difficult to interpret in that it does not provide any guidance on the magnitude of the benefits that should accrue to participants or their community. Moreover, it is somewhat confusing in that it suggests that researchers consider providing “health care,” but refrain from doing “aid work” without defining either term. It is therefore difficult to place it on the spectrum in this regard. The use of the word “should” is also problematic here and in other passages of the TCPS. It uses the word repeatedly without defining how strong of a prescription this is meant to be. Nonetheless, by endorsing clinical equipoise and to some extent, promoting the fair selection of subjects, I believe its approach is more Samplian than the previous two policies.
The Declaration of Helsinki is an international code of ethics for research involving human beings. Originally promulgated by the WMA in 1964, it has been amended several times, most recently in 2000 with “Notes of Clarification” added in 2002 and 2004. The CIOMS Guideline is intended “to indicate how the ethical principles that should guide the conduct of biomedical research involving human subjects, as set forth in the Declaration of Helsinki, could be effectively applied, particularly in developing countries” (CIOMS, 2002). Similarly, the UNAIDS Guideline is designed to accompany the Declaration of Helsinki and the CIOMS guideline, providing ethical guidance on issues related to HIV vaccine development.

I have grouped them together in this section because they fall into the same category with respect to their legal and ethical force. That is, unless the legislation or regulations of a given jurisdiction specifically refer to them, their legal force is limited. Campbell and Glass refer to this type of policy as “soft law.” They describe a Quebec case in which the court used the Declaration to define a physician’s obligation to disclose research-related risks, concluding that he had failed (2001). However, other courts have rejected the Declaration’s authority. For instance, the families of the victims of the Nigerian Trovan trial described in Chapter One ultimately sued Pfizer in the United States under the Alien Tort Claims Act. Supreme Court decisions relating to that law allow for claims based on evolving principles of international law. The plaintiffs claimed that the Declaration of Helsinki, the CIOMS Guideline and several other international
policies constituted such principles, but the court ruled that they are merely “a general statement of policy that is unlikely to give rise to obligations in any strict sense” (Abdullahi vs. Pfizer Inc., 2005). I am not aware of any litigation involving the UNAIDS Guideline, but given that its origins are similar to the Declaration and the CIOMS guideline, the courts would likely view it similarly.

However, the declaration is nonetheless seen as having moral authority. Glass and Lemmens write that it “is one of the most influential research ethics documents. It has proven to carry strong moral weight for health care professionals around the world, even in the absence of detailed national guidance or regulation” (2002, p. 476). Similarly, the Nuffield Council claims that, “…the Declaration is considered to be the pre-eminent guidance on ethical principles in research relating to healthcare” (2002, p. 60). Its moral authority has been challenged though, particularly the 2000 revision and subsequent footnotes. With regards to placebo controls, Robert Temple is quoted as saying, “I think it’s scientifically and ethically incorrect… We’ll have to see if the Declaration remains the ethical standard for the world” (Vastag, 2000). The CIOMS Guideline and the UNAIDS Guideline have received less attention than the Declaration, but they are regarded as having moral authority similar to it, since they are meant to be guidance on applying the Declaration in particular circumstances.

The Declaration contains strong provisions in all of the areas I have identified as Samplian. Article 19 specifies not only that research should not target vulnerable individuals, but that it should not be carried out in populations that are unlikely to benefit from it. The CIOMS and UNAIDS Guidelines have similar provisions in Guideline 10 and Guidance Point 4, respectively. Notwithstanding the ambiguity of the footnote, the
Declaration of Helsinki strictly limits when placebos may be used in research, and the CIOMS guidelines offer similar guidance with less ambiguity. Not surprisingly, placebo use is not an issue in the UNAIDS Guideline as presently there is no effective vaccine against HIV. Finally, these policies all contain provisions for post-trial access to treatment. The Declaration and CIOMS guidelines specify that negotiations should take place before a trial begins regarding what will be provided to participants after their involvement in the research. The UNAIDS Guideline goes further, stating that an effective vaccine should be made available not only to participants but to other high risk populations.

Thus, these documents are more closely aligned with Sample than the others I have considered. However, they do not appear to be legally binding, and while they have much moral force in some circles, it is easy enough for research sponsors to evade or abuse them.

**Reports from NBAC and the Nuffield Council**

The reports from NBAC (2001) and the Nuffield Council (2002) on the ethics of developing world research represent important contributions to the policy discussions in this area, and this chapter would be incomplete without some mention of them. However, they are not “policies” in the sense identified above, so they have been included separately in this section, which will briefly consider how they engage with the problem of exploitation. In contrast to the policies described above, these reports comment critically on the issues and offer thoughtful, nuanced recommendations to various parties.
involved in developing world research. However, they are not meant to be policy and it would be difficult to apply them as such. On critical issues, they often list important factors to be considered in judging the ethicality of a given study, but they stop short of setting a particular threshold. It is therefore more difficult to describe them as being aligned with Sample or Wertheimer, but where there are affinities this section will point them out.

As with the policies considered above, it is worth considering the degree to which they are influential and the source of their authority. Both reports make recommendations, but in neither case are these legally binding. Although NBAC was created by an executive order issued by President Clinton, its role was only “to provide advice and make recommendations to the National Science and Technology Council and to other appropriate government entities regarding the following matters” (Executive Order No. 12,975, 1995). Its recommendations are not binding though, and there is evidence that many of them are being ignored. For example, the NBAC report makes several recommendations as to how the FDA might improve the protection of participants in foreign studies. However, the FDA seems to be moving in the opposite direction in some cases, for example by dropping its requirement that foreign studies be conducted in accordance with the 1989 version of the declaration of Helsinki and replacing it with the weaker requirement that they comply with the ICH-GCP Guideline (Human Subject Protection, 2008). The Nuffield Council has even less prescriptive force. It is an independent think tank funded jointly by the Nuffield Trust, the U.K. National Research Council and the Wellcome Trust. Although it aims to influence policy, it has no governmental mandate to do so (Nuffield Council on Bioethics, 2005). This means that it
is free to address recommendations to the governments of developing countries, though
decisions on these issues are obviously the prerogative of the government in question.

Nonetheless, the importance of these reports should not be dismissed. According
to Eric Meslin and Arnold Shapiro, the Chairman of NBAC, the report placed
international research on the U.S. policy agenda for the first time (2002). In addition, the
papers commissioned by NBAC remain, in my opinion, among the most important
empirical studies on issues relating to developing world research. Finally, the stature of
the members of NBAC and the Nuffield Council, all eminent physicians, jurists and
 ethicists, and the fact that they came to a consensus on the content of the reports, suggest
that their recommendations ought to be seriously considered.

The NBAC Report

Although the NBAC Report does not discuss its meaning at length, several
passages illuminate what its authors might mean by “exploitation.” Echoing Sample, they
write that “exploitation in any form can be construed as a human rights violation by
virtue of its failure to recognize the inherent dignity of every human being, a precept
embodied in the Universal Declaration of Human Rights” (2001, p. 10). However, they
go on to say that, “it is important to ensure that the host country itself is not exploited and
that the rich and powerful do not appropriate an unfair share of the fruits of the research.”
This passage has elements of both Sample and Wertheimer. On the one hand, it suggests,
like Wertheimer, that the distribution of benefits arising from a transaction is crucial.
However, like Sample, it also allows that whole countries may be exploited and that the parties’ background conditions are relevant.

The NBAC Report takes a balanced stand on the three issues that I have identified as Samplian. With respect to representativeness, it states that “Clinical trials conducted in developing countries should be limited to those that are responsive to the health needs of the host country.” It holds that there should be a rebuttable presumption in favour of “established effective treatment” for any control group. This, Lurie and Wolfe noted in 2000, was somewhat weaker than the Declaration of Helsinki’s then-unequivocal requirement that they receive the “best current prophylactic, diagnostic, and therapeutic methods.” Nonetheless, it significantly limits the circumstances under which a placebo or no-treatment control would be deemed acceptable. Finally, NBAC concludes that research sponsors should make “reasonable, good faith efforts” (p. ix) to ensure that participants have ongoing access to needed treatments at the end of the study. For non-participants, they conclude that there should be prior negotiations regarding the availability of the treatment, but that the obligation to provide it should not be the sponsor’s.

The Nuffield Council Report

The Nuffield Council Report reaches conclusions very similar to those of NBAC on these three issues. However, it differs in that it explicitly discusses the meaning of

exploitation in the context of international research, listing the “duty not to exploit the vulnerable” as one of its central principles. Interestingly, the report explicitly invokes Goodin’s *Protecting the Vulnerable* (p. 52). However, they go beyond Goodin asserting that all those involved in health research have “roles and obligations” in “reducing global health inequalities” (p. 53). Their conception of exploitation appears to be broader than Wertheimer’s too. They claim that research should not assume that current conditions in the developing world are a morally acceptable baseline and that the communities in which research is conducted ought to receive some benefit too. These explicit claims about exploitation are more consistent with Sample than with Wertheimer.

The report goes on to discuss exploitation as a relevant consideration in the choice of comparator arms and post-trial benefits. With regards to the latter, Nuffield emphasizes the importance of prior negotiations and transparency. They insist strongly that participants who were randomized to a treatment found to be inferior should have access to the superior treatment if they still need it after the study. Nuffield is somewhat weaker with regards to ongoing access for participants with chronic conditions. They argue that this should be determined through prior negotiations, that there should be a presumption in favour of ongoing access, but that a local ethics committee may allow for exceptions to this presumption. Whatever the case, potential participants should be told how long treatment will be made available. Nuffield’s recommendation with regards to access for the host community is even weaker. They claim that while this is a laudable goal, it would be too heavy a burden to impose on research sponsors.

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12 It should be noted though that their report (2002) predates Sample’s book on exploitation (2003).
The authors define “universal standard of care” as the best intervention available anywhere in the world and argue that it should be the comparator by default. However, they note that this may not be feasible for practical reasons, and that in some cases, using the universal standard of care may not be appropriate because it does not allow the investigators to answer the relevant question. They conclude that the best intervention available through the host country’s public health system is the absolute minimum that would be acceptable. Initially, this appears to contradict their earlier claim that research should not take prevailing conditions as an ethically acceptable baseline. However, they claim that whether a given study is exploitative depends on the context. Even though a study uses the sub-optimal national standard as a comparator it may not be exploitative; providing that standard to participants does not necessarily tacitly accept that it is ethically adequate. By doing research that will lead to improved care investigators may actually be affirming their commitment to improving care, and thereby discharging their obligations. They write:

The Working Party is firmly of the view that the need to avoid exploitation is imperative… it is a fundamental ethical principle that those involved in research in developing countries should not take advantage of the vulnerabilities created by poverty or a lack of infrastructure and resources… the Working Party considers that insisting upon a universal standard of care may not always be the best way to respect this principle. (p. 90)

The term “taking advantage” is vital to this passage. It suggests that the crucial question in terms of exploitation is not strictly what participants in the comparator arm
receive. Rather, the crucial questions are, “Why is a sub-optimal comparator being used?” and “Who will benefit from the choice of such a comparator?” Research would rightly be considered exploitative if a sub-optimal comparator was chosen even though an optimal comparator would answer the research question equally well, but the main beneficiary of the research was the developed world. However, if the main beneficiary is the host community, the use of a sub-optimal comparator might not be exploitative.

To ensure that the host community is indeed the main beneficiary, Nuffield recommends that the governments of developing countries set up lists of priority areas for research. Research that falls outside of those priorities would require special justification to ethics committees in both the host and sponsoring country. Although, defining research priorities is clearly an important step for health ministries in developing countries, this important recommendation does not appear in the NBAC report. However, allowing local RECs to decide whether non-responsive research is nonetheless acceptable puts them in a difficult position, as will be discussed in Chapter Four.

**Guidelines from India and South Africa**

This discussion of exploitation and research ethics policies would be incomplete without a brief mention of the guidelines actually promulgated solely by developing countries. Although some of the international guidelines had input from developing countries, they are nonetheless a compromise with the interests of developed countries. An extensive analysis of these policies is frustrated by a number of factors. Firstly, over eighty countries, including many developing countries now have legislation, regulations
and/or guidelines on research (OHRP, 2008). It would be impossible to review them all in the context of this thesis. Moreover, many of these policies are not published in English, nor are there resources explaining how these policies fit into the national regulatory framework. Nonetheless, India and South Africa have English-language policies, though this is clearly too small a sample from which to extrapolate. Still, these countries are home to a significant amount of research and an analysis of these guidelines will shed some light on how they view research.

These policies deal with much of the same material as the others described above. However, the emphasis in these policies is somewhat different than their Western and international counterparts. For example, both South Africa’s Guidelines on Ethics for Medical Research (Medical Research Council of South Africa, 2002) and India’s Ethical Guidelines for Medical Research on Human Subjects (Indian Council of Medical Research, 2000) play down the placebo issue. The Indian policy reads, “Denial of the available treatment to control (placebo) group of patients is unethical” (p. 27). This obviously stops well short of Helsinki’s “best current therapeutic, diagnostic or prophylactic method.” South Africa’s policy doesn’t even mention placebo controls except for the matter-of-fact statement,

> It is normally necessary to compare the outcome in a large number of patients, some of whom receive the new treatment and some of whom receive standard treatment (control patients). Some trials may also require the use of inert or placebo preparations for comparison. (Section 4.2.3)

Instead, these policies emphasize the importance of justice and non-exploitation. The preamble to the South African policy notes that it has an “African outlook” on
research ethics and that it “emphasises the principle of autonomy- particularly from the perspective of ‘non-exploitation’ of research participants.” Under the heading “Principles of non-exploitation,” the Indian policy states that “as a general rule research subjects are remunerated for their involvement in the research or experiment” (p. 9). The South African document takes a somewhat different approach, stating that there must be “equitable compensation of institutions, investigators, participants and communities. This shall be beyond pure financial compensation” (Section 11.4.2) and mandates RECS to ensure that this is respected. Both policies also speak to the fair selection of participants. While the Indian policy states that less vulnerable subjects should be selected preferentially (p. 23), the South African one goes a step further, insisting that research be responsive to the health needs and priorities of the community in which it is conducted (Section 7.1). Likewise, the Indian policy is precise, but modest in its requirements for post-trial access to treatment. It states that “after the clinical trial is over, if need be, it should be made mandatory that the sponsoring agency should provide the drug to the patient till it is marketed in the country” (p. 27). Again, the South African policy is vaguer but apparently more generous, claiming that benefits should flow to the entire host community and that the research findings should be translated into practice (Section 11.4.4).
Conclusion

This chapter has surveyed a number of influential policies that guide the course of research. In this small sample, it has shown the policies that are more legally binding tend to focus on the well-being of participants during research, which, I have argued, is consistent with a Wertheimerian approach to research ethics. The policies that are more aspirational are more consistent with a Samplian approach.

Perhaps this is not surprising. The interaction with individual research participants can be seen as a discreet encounter and the Wertheimerian approach is to bracket it off from the social context in which it occurs. It is therefore relatively easy to formulate and enforce policy based on such an approach. In contrast, a Samplian approach resists such reductionism and challenges the assumptions of the dominant social norms. It would therefore be more difficult to base binding policy on such an approach. Taken together though, these policies create an uncomfortable situation which Lavery describes as follows:

What is left, particularly in the context of international collaborative research, is an awkward marriage between non-binding international guidelines with some reasonably legitimate claims to moral authority in the protection of human subjects and legally required regulations that some view as having diminished moral authority” (2004, p.324)

My analysis here has several limitations that are worth reiterating. Firstly, the policies considered here are only a small fraction of those that have been promulgated in
different jurisdictions, and I cannot guarantee that they are representative of the whole. However, the specific policies I have surveyed are very influential in their respective spheres and at the very least, my analysis suggests that there may be a trend and that a broader analysis would be warranted. Secondly, I have limited my analysis to an idealized research participant— a competent adult individual. In reality, participants are often children or mentally incapacitated adults; they are not just individuals but members of larger units like families and communities; and they are not androgynous persons, but men or women. If these factors had been taken into consideration a different conclusion may have resulted. Finally, I have focused on provisions pertaining directly to the benefits of research. Wertheimerian and Samplian analyses of other provisions, such as those pertaining to informed consent and independent review, might also prove interesting.
CHAPTER FOUR: BEYOND CODES OF ETHICS

Chapter Two of this thesis examined the concept of exploitation as it relates to biomedical research in developing countries, showing that there are important differences between different theorists’ understandings of exploitation. Chapter Three provided a close reading of various codes of ethics, attempting to extract the concept of exploitation that they envision. It concluded that while the more “aspirational” guidelines are more closely aligned with Sample’s philosophy, those with legal or regulatory force appear to take a Wertheimerian approach.

With this in mind, this chapter will consider the “moral weight” and “moral force” of exploitation. That is, it will ask, “How bad is exploitation?” and “What ought to be done about it?” To do so, it will summarize Wertheimer’s chapter on the subject and consider the extent to which his ideas on the subject are compatible with a Samplian view of exploitation. Next, it will apply Wertheimer’s ideas to the problem of exploitation in developing world research, with an analysis of what part RECs ought to play in dealing with exploitation. To facilitate this analysis, a description of RECs’ mandate as per the policies described in Chapter Three will be provided. Ultimately, this chapter will argue that taken together, these policies do not provide RECs with a strong mandate to prevent exploitation if the concept is understood in the broad Samplian sense. Moreover, RECs’ only options are to approve, reject or request changes to a study and no matter how they are exercised, it would do little to prevent such exploitation.
Finally, it will argue that factors beyond RECs’ control, in particular the funding of international research, contribute to the exploitation of research participants in the developing world. To make international research less exploitative, these factors would have to be addressed.

Moral Weight and Moral Force

Wertheimer (Again)

Chapters Two described various theorists’ conceptions of exploitation. While they all agree that exploitation is a morally charged notion, only Wertheimer devotes significant attention to what he calls “moral weight” and “moral force.” He uses these expressions to mean, “How bad is it?” and “What ought to be done about it?” respectively. It would be tempting to assume that exploitation is always seriously wrong, and that it ought to be prevented no matter what, but this would be too simplistic. Wertheimer devotes a whole chapter to the nuances of these questions (1996, p. 278-307) and a brief summary will be provided here.

Wertheimer begins by rehashing the classic liberal argument that there is a difference between that which is wrong and that which ought to be illegal. He points out that there are a number of viable reasons for the state to allow exploitative transactions even if they are wrong. Firstly, reasonable people can disagree with regards to what constitutes a fair transaction; if there are no objective criteria, it would seem futile to have the state try and resolve such a dispute. Secondly, in some cases the privacy of the parties
is a greater concern than the terms of their transaction. Finally, in some cases the freedom of being able to maximize their own self-interest outweighs the harm that results from exploitation. Thus, even if exploitation is bad, it does not necessarily follow that the state ought to prevent all instances of it.

If this is so, then the question of how bad exploitation is becomes all the more important. This question is complicated as there are a vast number of potentially exploitative transactions and there are good reasons to think they are not all equally bad. Wertheimer again limits himself to consensual, mutually advantageous exploitation, but this still leaves a wide variety of transactions. To account for this, Wertheimer proposes three criteria for determining how bad a particular instance of exploitation is. Firstly, he claims that it depends on the closeness of the relationship, writing that, “the relationship creates new possibilities, and A cannot simply insist that his actions be evaluated against the old standards, rather than the new ones” (1996, p. 191). Secondly, he claims that the wrongness of a transaction is proportional to the difference between the actual terms of the transaction and fair terms. Finally, he seems to suggest that the wrongness of an exploitative transaction is proportional to the degree to which A is responsible for B being in an unjust (or unfortunate) situation in the first place. He phrases this criterion in the negative though and does not elaborate on it: “even when B’s suffering is rooted in social injustice, it may (reasonably) be treated as a misfortune by A, if A bears no special responsibility for causing or alleviating B’s suffering.” (1996, p. 298)

Next, Wertheimer turns to the question of what ought to be done about exploitation. He is particularly concerned with whether and how the state ought to intervene to prevent exploitation, either by declaring certain kinds of transactions illegal
or by refusing to enforce them. He distinguishes between perfectionist intervention and strategic intervention.

He defines the former as interventions that aim to prevent exploitation for “moral reasons... that are not rooted in appeals to the non-moral interests of exploited parties or other vulnerable persons” (1996, p. 305). Perfectionist interventions, he claims, would be motivated by the belief that some transactions involve immoral activities and that society should prevent such transactions because they damage the “moral character” of those involved. However, he goes on to dismiss such interventions as overly paternalistic. He points out that if the individuals involved believe that participating in the transaction is in their best interests, the state should not second-guess them on moral grounds. He writes that, “because exploitation is a wrong against the exploitee, it would seem that society has no basis for prohibiting the wrong if the exploitee is prepared to allow the wrong to go through” (p. 309).

Instead, Wertheimer advocates “strategic intervention,” that is, interventions that aim to motivate whole classes of potential transactors to agree on fair terms. Strategic intervention could take three forms. If it is determined that the terms of a transaction are unfair, the state could, firstly, invalidate the transaction meaning that neither A nor B gets anything. Secondly, the state could determine what fair terms are and insist that A provide them to B. Thirdly, the state could proactively instate rules to set fair terms for transactions. Wertheimer suggests that this type of intervention is likely to be the most effective as it is the most pro-active, and it does not require as many case-by-case judgments. He cites minimum wage laws as a good example of this. If we accept that a certain minimum wage is fair compensation for certain types of labour, then enforceable
minimum wage laws minimize the possibility that those who do such labour will be paid unfairly low wages and thus exploited. However, such laws do not benefit everyone. For example, suppose an employer, A, cannot afford the minimum wage, and a potential employee, B, would be willing to work for less than the minimum wage. Both A and B would be better off if they were allowed to transact. Nonetheless, he argues that such measures are justified not because they benefit B, but because they benefit a whole class of people (low-skilled workers) who would be worse-off if there were no such law.

Wertheimer places a number of additional limits on when it would be appropriate to intervene. Firstly, he claims that intervention is only warranted when there is a breakdown in market conditions, for example, when a seller has a monopoly on a particular commodity. Secondly, the proposed transaction must be exploitative under current background conditions. (Recall that in Wertheimer’s framework, background conditions in a society may be unjust and this may mean that the market price of a particular good or service is unjust. However, the market price is, by definition, not exploitative.) Thirdly, the intervention must be cost-effective. Finally, the intervention should be undertaken because it will result in a net benefit and not because the state finds the proposed transaction morally repugnant.

Sample (Again)

Sample’s work focuses on the nature of exploitation and the types of transaction that should be considered exploitative. She does not devote much attention to “moral weight” and “moral force,” in those or other terms. Nonetheless, there are good reasons
to think that she would disagree with Wertheimer on these issues. Wertheimer claims that it would be overly paternalistic for society to interfere with transactions for moral reasons unless the material interests of the parties are at stake. Sample, however, places great weight on aspects of the person that are not material in nature. Recall that she lists three categories of interaction that disrespect people: those that are not sufficiently attentive to their flourishing and well-being; those that take advantage of past injustices; and those that commodify an aspect of the person that should not be commodified. However, she does not discuss how bad it is for interactions to fail to meet these criteria, nor does she discuss what ought to be done about it. In the discussion that follows though, I will allow that the state may be justified in intervening in transactions to protect both the material and non-material interests of its citizens.

Moreover, Sample would likely disagree with Wertheimer’s contention that exploitation is merely a wrong against the individual. As discussed in Chapter Two, Sample’s theory of exploitation is broader than Wertheimer’s in that it allows that the object of the exploitation claim can be an individual, but also larger groups such as communities and whole countries. If this is the case, Wertheimer’s argument that “perfectionist” intervention is overly paternalistic falls apart. Paternalism means that someone imposes his or her will on someone else without due consideration of that person’s wishes. However, if the object of exploitation is truly the whole community, then intervention by the state need not be seen as paternalistic. Indeed if the government is acting according to the community’s moral values to prevent exploitation of the community, then intervention seems entirely appropriate.
Unfortunately, much of this discussion has been speculative in nature, and ultimately it is not clear how and when Sample would advocate state intervention in exploitative transactions.

**Application to Research**

Wertheimer offers three criteria for determining how bad exploitation is, and they seem especially well-suited to an analysis of exploitation in research.

Firstly, he claims that the closer the relationship in which exploitation occurs, the greater the moral weight of exploitation. This point seems particularly salient in the context of medicine and biomedical research. Although exploitation can occur in a wide variety of interactions, there are reasons to think that it is worse in research. Firstly, research may involve deliberately carrying out risky invasive procedures on the participant’s body; the relationship is intimate in a way that many other relationships are not. Other potentially exploitative interactions may involve an exchange of goods, services or money, but these can be separated from the person in a way that his health and bodily integrity cannot (Jonas 1969). Secondly, professional standards bind physicians and other health care professionals and it could be argued that exploitation is worse when the exploiter is a member of a profession whose *raison d’être* is to treat disease and alleviate suffering. Society allows physicians to perform risky procedures because there is a compensating benefit for the patient and because they have the education, training and experience to perform them competently. However, this privilege comes with certain responsibilities, namely, the duty to act in the patient’s best interests (WMA, 2006); in
legal terms, it is a fiduciary relationship\textsuperscript{13}. Society has been reluctant to offer the same privileges to members of other professions, for example PhD medical scientists, in the absence of a comparable set of professional responsibilities.

Secondly, Wertheimer claims that the badness of exploitation is proportional to the difference between the actual terms of the transaction and fair terms. As discussed in Chapter Two though, determining what fair terms are can be quite difficult and Wertheimer’s “hypothetical market” is not an adequate mechanism. Nonetheless, some studies seem exploitative because participants don’t get a fair share of the benefits; if they received even less, it would be reasonable to say that the exploitation is even worse.

Finally, Wertheimer suggests that exploitation is worse when the exploiter contributed to the exploitee’s unfortunate background situation. It is worth considering the extent to which this is the case in research. In some cases, the would-be exploiter is directly responsible for the unfortunate background situation. For example, if a patient goes untreated because he or she cannot afford the necessary drugs, the maker of those drugs bears some responsibility for the patient’s predicament. If that company then takes advantage of the patient’s treatment naïveté by enrolling him or her in a clinical trial, the exploitation indeed seems worse. One could take this argument a step further and claim that exploitation is worse when one the exploiter is a member of a class that is collectively responsible for the exploitee’s unfortunate background conditions.

Wertheimer would likely object to this as he limits exploitation claims to parties to a transaction. However, Sample would likely be sympathetic to this approach, and it would

\textsuperscript{13} It should be noted that there is much debate as to whether the relationship between physician-investigator and patient-participant should also be regarded as fiduciary (Richardson & Belsky, 2006)
certainly resonate in the Marxist tradition, which views exploitation as embedded in an unjust class system (Wolff, 1999). While philosophically interesting such an argument would face a number of hurdles. Firstly, one would have to define the class of exploiters. Would it be limited to the pharmaceutical industry, or would it include the entire social and legal regime that sustains it? Secondly, even if such an argument could be developed cogently, it is not clear what practical implications it would have within a system of governance where research is evaluated on a study-by-study basis. Therefore, I will not pursue this line of reasoning any further.

Thus, Wertheimer’s work provides some valuable insight into the moral weight of exploitation in research. It also has important implications in terms of what ought to be done about this problem. He argues that in some cases, there are good reasons to allow exploitation even though it is wrong. In the context of research, his argument that individuals should be allowed to maximize their own interests is most relevant. For example, as discussed in Chapter One, there are cases where a person’s only way to get health care is to enrol in a research study. The study may result in significant social surplus, and if it isn’t shared fairly with participants, the study would rightly be characterized as exploitative. However, it is not clear that such research should be disallowed. From the point of view of the potential subject, even an exploitative study may be better than no study. In this case, it might indeed be paternalistic for an authority to prevent a potential subject from enrolling and deriving at least some benefit from it. Ultimately, Wertheimer advocates a pragmatic approach to intervention, arguing that it is most appropriate to intervene when doing so will benefit whole classes of potential exploitees.
What Should RECs Do?

The previous section summarized and critiqued Wertheimer’s argument that even though exploitation is wrong, the degree to which it is wrong varies and that it is not clear that all exploitative interactions should be disallowed. Wertheimer’s abstract discussion refers to intervention by “the state,” but in reality particular entities intervene on the state’s behalf. In the context of research, the state calls upon RECs to judge the acceptability of particular research studies. These committees function according to particular policies, some of which were mentioned in Chapter Three. One of the main purposes of these policies is to prevent the exploitation of research participants, though as discussed, the policies differ in their conception of it.

This section will consider the mandate of RECs under these various policies. It will argue that in view of the legal force of the policies, RECs have a strong mandate to prevent some forms of exploitation, namely those that involve the participants’ health and well being during the study. However, their mandate to prevent “Samplian exploitation,” for example by ensuring that studies are responsive to local health needs is much weaker. Moreover, it will show that the tools at the REC’s disposal, namely the power to approve, reject or request changes to studies can only accomplish so much in preventing this type of exploitation. Finally, it will argue that even if some RECs adopted a hard line on these issues, it would do little to improve the overall conduct of research.
The Mandate of RECs

Beginning in the early 1970’s, a series of research scandals ushered in the era of regulatory oversight in research and in 1981, the requirement for review by an ethics committee became part of U.S. law. Under that system, an institutional committee is responsible for oversight of research conducted in the institution, and research protocols must receive the committee’s approval before initiation (Emanuel & Grady, 2006). Since then, this system has been mandated by the many policies that govern research ethics, though as noted in Chapter Three, the policies are not always consistent with one another.

The policies vary in their vision of RECs’ mission. Appendix II reconsiders the codes of ethics discussed in Chapter Three, showing the passages most relevant to the mandate of RECs. These policies agree with each other insofar as they instruct RECs to protect the rights and well-being of research subjects by approving, requiring changes to, or rejecting research protocols submitted to them. However, they also vary in terms of how much additional discretion they give to RECs to approve or reject protocols on grounds other than the protection of subjects. At one extreme, the Common Rule explicitly instructs RECs not to consider the long-term consequences of research, stating that, “The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.” The ICH-GCP Guideline takes the middle ground, neither encouraging nor discouraging RECs to take a broad view of the ethicality of research. At the other extreme, the CIOMS Guideline appears to encourage RECs to consider all ethical issues arising from a
protocol. It stipulates that “the basic responsibilities of ethical review committees are... to ensure that all other ethical concerns arising from a protocol are satisfactorily resolved in principle and in practice” (CIOMS, 2002). The other policies fall somewhere along this same spectrum. As discussed in Chapter Three, the Common Rule is considered administrative law in the United States; the CIOMS Guideline, however, should be viewed as “soft law” as its legal force is not clear. Once again then, it would seem that the legally binding policies take a narrow approach to ethics, focused on participant safety, while the aspirational ones have a broader scope. In view of this, RECs may not feel compelled to interpret their mandate in the broad way envisioned by CIOMS.

To complicate matters further, research may have to be reviewed by RECs in both the host country and the sponsoring country. This is explicitly required by the TCPS and the CIOMS Guideline as shown in Appendix II. The TCPS focuses on Canadian researchers and their institutions. As mentioned above, it makes Canadian institutions accountable for research conducted under their auspices regardless of where it is carried out. It does not prescribe specific roles for each of these committees nor does it provide any further rationale for Canadian involvement in the review process. The CIOMS Guideline is more precise, specifying that the host country REC should ensure that the proposed study is responsive to local health needs and priorities.

The differences between the policies could lead to very different decisions on particular studies. For instance, an REC that strictly applied the Common Rule might approve a study that recruited participants in the developing world, even if most of the benefits from that study accrued to people in the developed world. However, an REC that applied the CIOMS Guideline strictly might disapprove the study on the grounds that this
is not representative of local health needs and therefore exploitative. It should be noted that in reality, RECs’ general functioning and specific decisions may deviate from the guidelines they are supposed to operate under. Studies have shown that they sometimes come to very different conclusions about the same protocol even though they are operating in the same regulatory environment (McWilliams, Hoover-Fong, Hamosh, Beck, Beaty, & Cutting, 2003). Still, I believe that a close reading of the text is of some value and it would seem there are some inconsistencies between them with regards to the role of RECs.

What Should RECs Do?

The preceding discussion argued that RECs legal obligation to reject research on grounds other than the rights and well-being of participants is relatively weak. However, this does not mean that RECs ought not to reject research that, for example, is not responsive to local health needs. This section will consider that question.

In making such decisions, RECs should think about what options are available to them and the likely outcomes of the different choices. As mentioned above, their main choices are to accept, reject, or require changes to research studies, though they may also try to persuade researchers to make changes without actually requiring them. In other words, they act as a filter, rejecting only the most objectionable protocols, but approving the majority. Unfortunately, they do not have Wertheimer’s preferred option, namely determining what fair terms of engagement would be and mandating that all transactions
conform to them. Their options are most similar to his least-preferred option, that is, deciding that the terms of a particular transaction are unfair and nullifying the transaction.

It should also be noted that there are certain practical constraints on these powers. For example, RECs may in theory reject any or all protocols submitted to them. In reality though, there may be great pressure on them not to reject too much research. Although RECs are supposed to be free of conflicts of interest, they rarely are. REC members are usually employees of the institutions the committee serves and often colleagues of the investigators whose studies are reviewed. Furthermore, research is an important part of many medical centres’ missions, and their reputations, as well as their balance sheet, may hinge on the quality and volume of research that takes place within their walls (Macklin, 2008). REC members may therefore feel pressure to create a research-positive environment, even if they have reservations about some studies.

This is especially so in developing countries, where as Petryna points out, research is perceived as a social good in itself. In this context, approving research is not merely a matter of the institution’s prestige, but of what it can offer to desperately sick patients. In other words, the REC may be placed in a position of having to decide whether patients will have access to an experimental treatment (albeit one that is not responsive to local health needs) or no treatment at all. These pressures on developing world RECs may account for the fact that they are somewhat more permissive than their counterparts in the developed world. For instance, NBAC found that “ethics review committees in developing countries were less likely to raise either procedural or substantive issues for a given study, compared to U.S. boards” (2001, p. 82). They also found that in some cases the very requirement that studies be reviewed by an ethics committee was put in place
merely to comply with U.S. regulations, suggesting that their commitment to the process may be less than optimal (2001).

In addition to rejecting studies, RECs also have the power to request changes to a protocol. However, if these changes are unacceptable to the investigator or the sponsor, they are free to withdraw the study. That is, RECs can request, but cannot demand changes to the study. The degree to which sponsors and investigators are willing to change their studies in response to REC requests depends on a number of factors. They may be particularly unwilling to change the study if it will adversely affect its scientific validity. Multi-centre clinical trials, for example, must be conducted according to the same parameters at all sites; the sponsor may be better off excluding a site rather than accommodating it.

Regardless of the constraints placed on RECs and regardless of how legitimate they are, RECs still theoretically have the power to reject or require changes to a study. The question, again, is whether they ought to. As discussed above, legally binding policies leave RECs little leeway where the well-being of research participants is concerned. If studies are excessively risky, for example, or if the process for obtaining informed consent is inadequate, RECs have little choice but to reject them. They seem to have more latitude with studies that are attentive to participants’ well-being but are not responsive to local health needs, and with studies in which there is no post-trial access to treatment.

Contrary to CIOMS, I believe that RECs would be justified in approving some such research. Although rejecting such studies might make a statement to the effect that the institution wants to promote justice in research, it is not clear how effective such a
statement might be. In Wertheimer’s terms, RECs are not in a position to set policy that would improve conditions for a whole class of B’s. After all, it would not prevent sponsors from doing such research; they would just have to find another site. Moreover, rejecting unresponsive research would in no way guarantee that responsive research would be carried out. And finally, the decision to reject such research could end up harming the institution’s patients; it might mean denying them access to an effective treatment, albeit an experimental one. Thus, the REC’s may have to decide which principles carry more weight in a particular situation. In simplistic terms, allowing such a study would place more weight on autonomy and possibly beneficence while rejecting it would place more weight on justice. This is consistent with Beauchamp and Childress’ principle-based approach to Bioethics; they “construe principles as prima facie… The latitude to balance principles in cases of conflict leaves room for compromise, mediation and negotiation” (2001, p. 405).

In some cases then, Wertheimer’s argument that disallowing certain types of transactions is overly paternalistic may be convincing to the REC. For example, in the Milan study described above, it would seem highly paternalistic for an REC to prevent the parents of the Colombian and Palestinian children with ADA-SCID from pursuing an experimental treatment for that condition. Moreover, disallowing that research protocol would not have done anything to ensure that the child did receive conventional treatment. As described by Kimmelman (2007), there are several reasons to be uncomfortable with this study, but it does not follow that RECs ought to reject it.

However, in other cases, RECs seem justified in disallowing certain research on the grounds that it is not responsive to local health needs. Fitzgerald and Wasunna
describe an example in which a sponsor proposed a study of a drug for sepsis that was to be conducted in Haiti (2006). The drug was evidently being developed for use in sophisticated intensive care units in developed countries; Haiti has no such units. However, the sponsor proposed to test the drug in general medical units, where the prognosis for sepsis is very poor regardless of what treatment is offered. Thus, although the study might have given participants a slightly better chance of survival, the investigator decided that the study was so unresponsive to local health needs that it should not be conducted in that setting. Although this study never made it as far as an REC, I believe they would have been justified in turning it down.

In conclusion, this section has shown that RECs are severely constrained in their ability to prevent Samplian exploitation. Their mandate to do so is weak, they face certain political obstacles and the tools at their disposal are not well-suited to the task. Given these limits, their best strategy may be to use their powers judiciously and adopt an approach that balances their duty to maximize benefits against their duty to prevent exploitation. In some cases this may mean approving studies that are not responsive to local health needs.

**The Role of Research Funding**

Henry David Thoreau said, “There are a thousand hacking at the branches of evil to one who is striking at the root” (1854). Although the word “evil” seems much strong in this context, intervention by RECs seems too much like hacking at its branches. We should also ask what the root cause of exploitation in developing world research is. In
this section, I will argue that the financing of research is the source of the problem and that the solution must involve a radical change in its funding.

Funding in the Private and Public Sectors and the Resulting 10/90 Gap

Health research has become a very important part of the economy, but spending in this sector is grossly skewed towards conditions that afflict the developed world. This is not unusual; spending in other sectors is similarly skewed. However, it is somewhat disappointing in an endeavour that lists “justice” as one of its guiding principles. This section will briefly describe the “10/90 Gap,” and explore the economic forces that create.

Work from the early 1990’s first described the discrepancy between the global burden of disease and the allocation of research resources. At the time, worldwide spending on health research was about $30 B, annually but only about 5% of that went to diseases that were responsible for 93% of the years lost to premature death, diseases that are only prevalent in the developing world (Commission on Health Research for Development, 1990). Although spending on health research has ballooned to over $125 B since then this pattern persisted through the 1990’s and led to the Global Forum’s 10/90 Reports on Health Research. The last report was published in 2004, and the Global Forum now believes that the burden of disease in developing countries has shifted towards non-communicable diseases, making it impossible to quantify the proportion that is allocated to the concerns of the developing world. Nonetheless, they write that “health research applied to the needs of developing countries remains grossly under-resourced in
many areas and the term ‘10/90 gap’, while not representing a current quantitative measure, has become a symbol of the continuing mismatch between needs and investments” (Global Forum for Health Research, 2008).

It would be an oversimplification, however, to treat global spending on health research as a pie that can be cut into pieces of any size and distributed to any part of the world. In reality these funds come from particular sources— the largest are pharmaceutical companies and governmental agencies from developed countries. These organizations are not mandated to promote global justice or rectify the health inequalities that separate the rich from the poor. Pharmaceutical companies’ mandates, ultimately, are to maximize shareholder value by developing and marketing safe and effective treatments for disease. To do so, they must develop products for which there is a market, and the largest markets are North America, Western Europe and Japan. In light of this, it seems unreasonable to expect them to invest in areas that are less than optimally profitable, such as drugs for use in the developing world. It might be more reasonable, though, to blame Western governments (and their electorates) for failing to create a market for such products through strategic incentives.

Likewise, governmental agencies that fund health research are ultimately accountable to the electorates of Western democracies. It is not surprising then that their mission is to fund research that will, in the end, benefit these populations. For instance, the CIHR describes its activities as follows: “As the major federal agency responsible for funding health research in Canada, the Canadian Institutes of Health Research (CIHR) supports more than 10,000 researchers and staff each year. Together they are challenging the frontiers of science in order to increase our knowledge and understanding of health
sciences and ultimately, to improve the health of Canadians” (CIHR, 2004). Although the CIHR has a Framework for International Relations and Cooperation that aims to “address internationally recognized priorities in global health research,” (CIHR, 2006) this program preferentially seeks collaboration with international partners when there is an anticipated benefit for Canadians. With regards to partnerships with low-income countries, it prioritizes initiatives in the area of “emerging health threats,” such as SARS and HIV that could directly affect Canadians. Similar statements hold for the U.S. NIH’s mission and approach to international collaboration (NIH, 2007). In the case of U.S. researchers working in developing countries, the granting agencies’ funding priorities have indeed translated into research that is not optimally representative of the host country’s needs. A survey revealed that forty percent of them felt that these priorities were “incongruent with the top priorities of the developing country in which they worked” (NBAC, 2001, p. 20).

The skewed pattern of research spending described by the Global Forum and others raises two distinct issues. The obvious one is that of distributive justice, that is, is it fair that such a large portion of the money spent on health research should be devoted to the health concerns of those who already enjoy a relatively high standard of living? In my opinion it is not, but an analysis of this phenomenon under various theories of distributive justice is well beyond the scope of this chapter. I submit though that such an analysis should take into account the likely payoff (in terms of alleviating suffering) that would result from spending in different areas. Whereas clinical research on chronic conditions that afflict the developed world is facing diminishing returns on investment, research on many conditions prevalent in the developing world could be translated into
effective clinical interventions relatively easily. For example, Millet points out that the basic science research on conditions like trypanosomiasis and leishmaniasis has been very fruitful and translating it into clinical interventions would be relatively easy. However, neither industry nor the public sector has been willing to invest in doing so (2006). It should be noted that even if clinical research showed that a certain drug was safe and effective, this would not guarantee that it would be made available to those who need it. Nonetheless, such research would represent a step forward in that if a particular drug was on the market, governments and the private sector might be able to bargain with the pharmaceutical industry to make it available at a reasonable price, as they have done for fixed dose combinations of HIV/AIDS drugs (Kaiser Family Foundation, 2004).

The second issue is that while 90% of research targets the problems of the developed world, it is often conducted in developing countries and may not be responsive to their health needs. It may be unresponsive, in that it investigates a condition that is not an important health priority in the jurisdiction where it is conducted. There are several examples of such research in the bioethics literature: the ADA-SCID trial discussed above; a proposed study of Surfaxin to be conducted in Bolivia (Lavery et al., 2007, p. 151); and the proposed study of a sepsis drug to be conducted in Haiti described above. To my knowledge though, there is little empirical evidence to show how widespread this phenomenon is. Nonetheless, these studies were not responsive to the health priorities of these communities, though it should be noted that responsiveness has not been adequately explored in the bioethics literature (London, 2008). There is also much ethical debate as to what the ethically relevant community is in this context (Arras and Crouch, 1998).
Still, I submit that the examples cited above are unresponsive and therefore exploitative as discussed in Chapter Three.

Research may also be unresponsive in that it tests a treatment for a condition that is an important health priority, but the treatment itself is not well-suited to the context in which it is being tested (London & Kimmelman, 2008). Indeed, it is the often prevalence of particular diseases and availability of treatment-naïve patients that make certain countries attractive as recruiting sites. These sites are often in middle-income countries such as Brazil and Poland (Petryna, 2006), countries whose burden of disease is skewed towards chronic conditions, but whose health systems are less than optimally equipped to handle them. Research conducted there might test an intervention that requires extensive medical monitoring that is not widely available in the area in question. Similarly, it might test an intervention that will be unaffordable to the population in which it is tested. This was an issue in the trials of AZT to prevent perinatal transmission of HIV from mother to child. Notwithstanding the ethical issue raised by placebo use, these studies showed that low-dose AZT reduced the risk of transmission. However, even though the low-dose regimen was much cheaper than that used in the developed world at the time, it was still out of reach of most people in the communities in which the research was conducted (Arras & Crouch, 1998), and indeed this treatment was still only available to an estimated 11% of those who need it in low- and middle income countries in 2005 (WHO, UNAIDS & UNICEF, 2007).
Surprisingly the literature on this phenomenon is sparse. However, the off-shoring of clinical research is well-documented\textsuperscript{14}, as is the widespread lack of access to patented pharmaceuticals in developing countries (Mendis et al, 2007). What is missing, to the best of my knowledge, is a study investigating where clinical trials are conducted versus where the products become widely available. Although Volume II of the NBAC Report investigates this issue, it does so by surveying researchers about what they intend to do at the end of research. It does not look at whether treatments actually became available. I suspect such a study would show a substantial gap and as argued in Chapter Three, this research should also be considered exploitative.

**Conclusion**

As discussed in Chapter Three, research ethics policies aim to prevent the exploitation of participants and the more aspirational ones embody a more plausible account of exploitation. Unfortunately, however well-intentioned these policies may be, there are structural barriers to their implementation. In this chapter, I have described how the funding mechanisms in health research lead to studies that are often unrepresentative of the health needs of developing countries. RECs as they are presently constituted are not in a position to fix this problem, and I have argued that they are justified in approving some research even though it is exploitative in the Samplian sense. Ultimately, funding is the cause of unresponsive research and changes must be made at that level to bring about

real improvements. As London writes, “We must move away from an over-reliance on
the largely reactive IRB review mechanism toward a more proactive model in which
issues of justice are considered much earlier in the research process” (2005).
CHAPTER FIVE: CONCLUSION

Summary

The exploitation of participants is an important concern in biomedical research, especially when it is carried out in the developing world. Although many codes of ethics aim to prevent exploitation, the bioethics literature has not thoroughly examined differing theories of exploitation and how they relate to biomedical research, particularly in the developing world. This thesis has attempted to bridge that gap. Chapter One of this thesis explored the recent growth in research in the developing world and the potential for exploitation that it creates. Chapter Two analyzed Goodin, Wertheimer and Sample’s theories of exploitation, applying them to the research context. Wertheimer’s theory holds that exploitation is merely an unjust distribution of the “social surplus” arising from a transaction. This chapter argued that this definition is too narrow, and that Sample’s, which construes exploitation as a lack of respect for a person’s true value, is superior. Chapter Three analyzed several influential codes of ethics, attempting to extract the concept of exploitation that they embody. It showed that while all of these policies were somewhat mixed in their conception of exploitation, those with legal force tend to take a Wertheimerian approach and more aspirational codes are more closely aligned with Sample. Chapter Four considered the limits of what RECs can accomplish by applying these codes of ethics and argued that the current system of research oversight cannot adequately deal with exploitation in international research.
Overall, this thesis draws attention to the importance of avoiding exploitation in developing world research and the importance of clearly articulating what is meant by exploitation. It considered some controversial issues in research ethics, namely placebo-controls, responsiveness and post-trial access to medications, and how these issues relate to exploitation. However, it has not attempted to integrate these considerations into a system for determining whether it is unethical to conduct a given study in a particular setting on the grounds that it is exploitative. Nonetheless, it would seem that these factors must be considered in combination with each other. For example, it would be very difficult to justify conducting a study that meets none of these criteria, that is, one that uses a placebo control, is not responsive to local health needs and does not offer any post-trial benefits to participants or their community. However, if a study were highly responsive to local needs, and the results could easily be translated into practice using existing infrastructure, it might be acceptable to use a placebo-controlled design if that was the only one that would answer the relevant scientific question. This is consistent with the Nuffield Council’s opinion that, “the need to avoid exploitation is imperative…” but that “insisting upon a universal standard of care may not always be the best way to respect this principle” (p. 90).

Consultation: A Necessary Step

Clearly, the potential for exploitation is greatest in research that is not responsive to local health needs and priorities, though there are many open theoretical questions on what responsiveness means. It would be too simplistic to assume that the most prevalent
diseases in a community are automatically the priority and that any research on these conditions is therefore responsive (Resnik, 2001). Indeed, this would be paternalistic; it makes unjustified assumptions about the community’s values and priorities and presupposes that the outside sponsor or investigator knows best how to engage with the problem.

For research to be responsive, it must take community members’ point of view into account. For this reason, many international ethics guidelines recommend a process of consultation with local populations before research is undertaken. The CIOMS Guideline is typical of them. It reads, “When an investigational intervention has important potential for health care in the host country, the negotiation that the sponsor should undertake to determine the practical implications of “responsiveness”, as well as “reasonable availability”, should include representatives of the communities from which subjects are drawn and non-governmental organizations such as health advocacy groups” (CIOMS, 2002). This type of negotiation may be of some value if the sponsor and investigator are committed to the process, if they are in a position to negotiate provision of the intervention on an ongoing basis, and if neither party attempts to abuse an advantage in bargaining power. In reality though, this is rarely the case. As discussed in Chapter Four, neither pharmaceutical sponsors nor Western granting agencies have a mandate to provide treatment on an ongoing basis. Moreover, the sponsor often has a bargaining power advantage in that they can set up trials at any number of sites, and will likely use the ones that are most expeditious. In contrast, if a particular site is too uncooperative, the sponsor can simply move on. It is not so easy for communities in the
developing world to walk away from the table; they may be inclined to accept terms that are less than fair but better than nothing.

Another weakness of this type of negotiation is that it takes a particular intervention for a particular condition as its starting point. Thus, some of the parameters of the negotiation are already set by the time the community is approached. I believe that if consultations were started earlier in the research process, they would be more likely to yield studies that are representative of local health needs. A study by Casapia, Joseph and Gyorkos (2007) provides an example. These investigators conducted multidisciplinary participatory workshops in an extremely poor community in the Peruvian Amazon. In the first, participants developed a ranked list of priority health concerns for their community, such as infant malnutrition, adolescent pregnancy and acute diarrhoeal illness; in the second they discussed potential interventions that they felt would be appropriate to deal with these concerns, as well as barriers to implementing them. Interestingly, most of the interventions they proposed “aimed to modify existing programs and infrastructure to better reach vulnerable populations” (p. 6). Thus, it seems that research was not a priority at all in this particular community, though it is not clear whether research was even discussed as a potential way meeting their needs. Nonetheless, one can imagine that in some communities research might be a priority, for example if the main barrier to implementing an intervention was lack of knowledge about its safety and efficacy in that population. If the call for research came from this sort of consultation, it would be far more representative of the population’s needs.

The results of such consultations might prove surprising though; they might reveal that there is little appetite for research. For instance, given the devastation the
disease has caused, one might assume that communities in sub-Saharan Africa are desperate for a vaccine against HIV and would be eager to participate in research on one. However, this is not necessarily their first priority. Stephen Lewis, the former U.N. Special Envoy to Africa for HIV/AIDS recounts an encounter he had with an AIDS victim in Zambia. Although this young woman desperately needed antiretrovirals to survive, when asked, she said that clean drinking water was what she needed most desperately (2005). This echoes Flory and Kitcher’s comment that, “most of the countries where malaria, tuberculosis, respiratory infections, diarrhea, parasitic infestations, and so forth are rampant owe their trouble not to the lack of twenty-first century medical technology but to the absence of late nineteenth century sanitation” (2004). If it turns out that consultations reveal that research is not a priority at all, then this should be taken seriously.

**Some Positive Guidance**

Thus far, this thesis has focused on avoiding exploitation. While doing so is a worthy goal, it is not the whole story. It does not show what international research ought to strive for. However, there is some work that aims to provide “positive guidance” to the research community and this section will summarize a selection of this work.
The “Engagement Principle”

Fitzgerald and Wasunna postulate that “Engagement” is the polar opposite of exploitation and that researchers should strive for it. They define it as follows:

“Engagement occurs when researchers and people in resource-poor communities work together in a just way to improve the health of the host community and to decrease unfair health inequalities” (2006). This principle is derived from Rawls’ *Theory of Justice* which holds that “social and economic inequalities in a society should be arranged so that they are both (a) to the greatest benefit of the least advantaged and (b) attached to positions and offices open to all” (1999, p. 53).

If we accept Engagement as a worthy goal, it allows us to criticize neglecting the health needs of developing countries in a way that we could not if we rely exclusively on non-exploitation. Fitzgerald and Wasunna take the example of syphilis, which is no longer a major health concern in developed countries and therefore not the subject of much research. Nonetheless, it remains a major health concern in much of the developing world. Not doing research on this condition does not constitute exploitation, nor does it contravene any of the policies aimed at preventing exploitation. However, Wasunna and Fitzgerald criticize it as follows: “we believe that this neglect contributes to global inequalities in health and is thereby morally wrong” (p. 562).

Fitzgerald and Wasunna’s article offers a brief introduction to engagement as a principle to guide the research community in setting ethical goals. I believe that applying Rawls’ theory to justice in research is a promising approach that merits further exploration. However, the article is quite short and it leaves many issues unaddressed.
Firstly it defines exploitation and engagement as polar opposites, with neglect falling somewhere in between. However, they do not discuss how strong of a “duty of engagement” researchers may have; it is not clear what extent research must engage with developing world communities for it to be acceptable. In addition, it does not provide guidance on how to operationalize that duty. While they suggest that engagement be written into international ethical guidelines, for the reasons discussed above, this may not be adequate.

*The “Human Development Approach”*

Alex London’s “Human Development Approach” offers similar positive guidance to the research enterprise (2005). He begins, however, by describing and critiquing what he calls the “minimalist position,” which he claims is the dominant approach to research ethics today. The minimalist position places great emphasis on the principles of non-maleficence, beneficence, and autonomy, but neglects justice. Where international research is concerned, this leads to the conclusion that research must leave participants and their community better off than if the research was not conducted; to insist on a higher standard would be to interfere with the autonomy of the community and the individual.

London cites the Participants in the 2001 conference on Ethical Aspects of Research in Developing Countries as proponents of the minimalist approach. The Participants were strongly influenced by Wertheimer, and the minimalist approach is quite similar to his philosophy. In particular, the minimalist approach views research
participation as a transaction and judges its permissibility by the distribution of the benefits that arise from it. London’s portrayal of the minimalists is somewhat unfair though: he claims that a minimalist would only insist that the benefits to participants and the community surpass the no-transaction baseline. In reality, both Wertheimer’s hypothetical market approach and the Participants’ fair benefits approach assume that the benefits to the exploitee are better than the no-transaction baseline. As discussed above though, the hypothetical market approach is unreliable and Ballantyne points out that the Participants’ definition of fairness is ambiguous at best (2008).

London points out three weaknesses to this approach. Firstly, it “accepts the status quo as the appropriate normative baseline for evaluating international research initiative” (p. 27). He claims this is inadequate because the population in a host community may have a legitimate claim to something better than that. He does not elaborate extensively on how such a claim might be grounded, except in the special case where there is a “duty of rectification,” that is where the researcher or his or her sponsoring entity is directly responsible for the poor health of people in the developing world. He argues that in such cases this duty of rectification is quite strong. However cases in which researchers or their sponsoring entities directly brought about the poor health of people in the developing world are rare. Rather, poverty and poor health in the developing world are the result of a constellation of natural and human causes (Sachs, 2005, pp. 51-75) and in most cases researchers and their sponsoring entities are only indirectly responsible for the situation, and only to a small degree. An argument based on distributive justice, that is, a general duty to bring about greater material fairness, might have been more convincing here. Secondly, the minimalist approach fails “to situate the health needs of individuals in
the developing world within a broader social, political and economic context” (p. 28). And thirdly, “because it limits its scope to this one activity [a particular research project], abstracted from its social, political, and economic context, it in effect treats any consideration of the character and quality of the basic social structures in the host community as unnecessary” (p. 28).

As an alternative, London proposes the “Human Development Approach.” Though he doesn’t cite Sample, this approach seems quite similar to hers in that it considers research in its broader context and views participants as inextricably linked to their communities. Like Fitzgerald and Wasunna, London suggests that research be judged by its potential to narrow unjust global health inequalities. Unlike the minimalists, London places great emphasis on existing social structures in the host community, in particular their healthcare infrastructure. The crux of his argument is the following:

The human development approach holds that collaborative research initiatives are permissible only if they are a part of, or contribute to, a fair social division of labor in the host community. In particular, they must directly and indirectly expand the capacity of the host community’s basic social structures either to meet the distinctive health priorities of that community’s member or to meet their basic health needs under distinctive social or environmental circumstances. (p. 33)

Echoing “Exploitation as Degradation,” London writes that human development must “guarantee to community members the fair value of their most basic human capacities.” Finally, London acknowledges research conducted in the near to medium term is unlikely to meet his human development standard. This leaves open the question
of what post-trial obligations investigators have to their participants in studies that do not aim to minimize health inequalities. As an initial answer, London proposes that these obligations are inversely proportional to the community’s ability to translate research results into meaningful improvements on its own.

Like Wasunna and Fitzgerald, London articulates his vision of the direction international research should take. He agrees that REC review is reactive and that it is not the ideal mechanism for promoting justice in research. Unfortunately, he has few concrete suggestions as to how to implement his vision, except to note that his article may serve as a guide to investigators and funders as to what research ought to be done.

*The “Identification Standard”*

Finally, I will summarize some of Hans Jonas’ arguments and apply them to the ethical problem of research in the developing world. Jonas’ influential work, “Philosophical Reflections on Human Experimentation,” predates the Belmont Report and the era of globalized health research. Nonetheless, his thinking (though perhaps not his writing style) seems remarkably fresh and relevant to today’s problems in bioethics (1969).

Jonas begins by considering what society owes to future generations and whether society ought to pursue continual medical progress. He concludes that medical progress, though it is a noble goal, is ultimately gratuitous. He writes, “If cancer, heart disease, and other organic, noncontagious ills, especially those tending to strike the old more than the young, continue to exact their toll at the normal rate of incidence… society can go on
flourishing in every way” (p.227). This is a radical point of view: it is usually assumed that research is some kind of “moral imperative,” but Jonas argues convincingly that it is not. He does, however, distinguish between research under ordinary circumstances and research under extreme catastrophic circumstances, such as Europe’s Black Plague.

Apparently referring to developing countries, he writes, “The life-sapping ravages of endemic malaria or sleeping sickness in certain areas are a public calamity of the chronic kind. A society as a whole can truly not “afford” such situations, and they may call for extraordinary remedies, including, perhaps, the invasion of private sacrosanctities” (p. 228). Here, he is suggesting that such circumstances might justify compelling people to participate in research. Clearly this is controversial, but a discussion of it is beyond the scope of this thesis. I would only say that the HIV/AIDS epidemic in sub-Saharan Africa has had a cataclysmic impact comparable to the Black Plague and that if ever extraordinary circumstances justified such an intervention, it would be there. However, the issue may be academic: it would seem that desperation has created a surplus of willing volunteers and that active coercion has not been necessary.

Here, I am more concerned with non-emergency research. If Jonas is correct and research is morally optional, under what circumstances is it permissible? Jonas turns to the “Identification Principle” to answer this question. He claims that research is permissible in proportion to the degree to which participants identify with its goals. The ideal research participant, he claims, is the investigator him- or herself. After all, no one is likely to understand an experiment as well as the investigator, and no one has as strong of an interest in its outcome. He concedes that the scientific community will never have the numbers necessary to meet the demand for research participants, allowing that one
should then, “look for additional subjects where a maximum of identification, understanding, and spontaneity can be expected- that is, among the most highly motivated, the most highly educated, and the least “captive” members of the community” (p. 235).

At face value, this seems elitist, particularly with regards to recruiting only well-educated participants. It also seems impractical; it would require an objective test to determine how much a potential participant identifies with the goals of the study. Of course, the test would have to be different from one study to the next, which would place an unreasonable burden on the investigator. However, I believe that the principle behind it has important implications for research in the developing world. As discussed in Chapter Three, patients may have many motivations for participating in research, notably they may hope that an experimental treatment will offer them a cure. However, they may also be motivated by altruism to some degree; they hope that through their sacrifice, future patients will have a better fate than them. That altruism seems plausible to the extent that the participant has something meaningful in common with the future patient. However, where research is conducted in poor countries and the main beneficiaries are in rich countries, it does not seem reasonable to say that the participant can identify with the research. Under these, circumstances, the “identification standard” has likely not been met.

Jonas’ identification standard would be especially useful if applied at planning stages of research. In deciding where to conduct a particular study, investigators could begin by considering the desired outcome and what populations would be most likely to identify with it. The identification standard also has important implications for informed
consent. Informed consent forms often go into great detail about the risks of participating in a study with relatively little attention paid to how the study may affect medical practice in the future. They typically contain a clause informing potential participants that they may or may not benefit from being in the study but that future patients may benefit from what is learned. Clearly, it would be difficult for a potential participant to decide if they identify with the goals of the research based on such vague information. It would be much more meaningful if the form discussed how the results of the research would be translated into practice in the local community. If there is no plan to do so, or if the plan is contingent on the outcome of the research, this should be disclosed forthrightly.

This points to the need for “positive guidance” for researchers and funders and the bioethics literature has provided little. Nonetheless, the work of Fitzgerald and Wasunna, London and Jonas offers some insight. Their emphasis on justice in health research, and specifically their claim that research should aim to minimize global health inequalities appear promising. The theoretical underpinnings of this approach need further development though and it should be noted that only so much can be accomplished by theorizing. Change will also require that the theory be operationalized through policy initiatives. This, however, cannot occur unless there the political will exists to bring it about.
Limitations and Future Directions

This thesis has covered a large amount of material in a relatively few pages and consequently, it has not gone into as much depth as it might have. It is therefore worth recapping some of its major limitations and pointing out where additional work is needed.

Firstly, I have focused on two theories of exploitation—Wertheimer’s and Sample’s—the former because it has become influential in research ethics and the latter because it offers a more tenable alternative. Other authors have written on exploitation, some extensively, and an analysis of their work as it applies to health research might prove fruitful. In particular, I have suggested that a Marxian examination of this issue would be of interest. Another theoretical issue that I have not addressed is the relationship between exploitation and justice; while related, these concepts are not equivalent. Does non-exploitative research necessarily bring about greater justice? Is it possible for research studies to exploit participants while contributing to justice? These questions remain unanswered here.

Secondly, I have limited my discussion to a relatively small number of research ethics policies and focused on particular clauses in them. It would be well worth repeating this analysis with a broader selection of policies and a more comprehensive scope. Nonetheless, I believe that by focusing on the clauses relating to benefits, which happen to be some of the more controversial ones, we begin to see that the aspirational guidelines take a more Samplian approach.

Finally, Chapter Four made a number of claims about the countries in which research is conducted and the countries that benefit from it. While these claims are
supported by anecdotal evidence, expert accounts and some empirical studies, they would be more credible if they were backed up by more systematic evidence. An interesting study might be to compare the countries in which clinical trials are conducted to the countries where the drugs become routinely available. On the other hand, such a study might reveal that no gap exists between where clinical trials are done and where successfully tested products become available. This would be cause to reconsider many of the conclusions I have drawn here.

**Conclusion**

To conclude, I would like to draw attention to the striking parallels between the ethics of recruiting human participants for research and the ethics of drafting individuals into the military. Both Wertheimer and Jonas comment on the latter issue. In typically detached style, Wertheimer writes, “Consider, for example, the decision of a low-income person to enlist in the military... It may be argued that the recruit’s poor background circumstances “force” the recruit to join the military- given the range of options, the recruit has no other acceptable choice” (p. 27). He goes on to argue that the lack of viable alternatives does not in fact constitute coercion and enlisting people in dire circumstances does not constitute exploitation. In stark contrast, Jonas writes, “we… feel morally disturbed if the draft, either by design or in effect, works so that mainly the disadvantaged, socially less useful, more expendable make up those whose lives are to buy ours.” Evidently, recruitment, both for research and for the military, raises disturbing ethical dilemmas. In trying to resolve them, it would be tempting to focus on the
relatively tractable issue of how not to exploit the individual as Wertheimer does.

However, as Jonas points out, the moral dynamics of recruitment for research go beyond the individual. There are implications for the countries and communities in which it is conducted and for those who benefit from it. These considerations create a challenge for research ethicists, but also an opportunity to think beyond the walls of the REC conference room.
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## APPENDIX I: CONTROVERSIES RESEARCH ETHICS- WERTHEIMERIAN AND SAMPLIAN ANALYSES

<table>
<thead>
<tr>
<th>Problematic Research</th>
<th>Does it exploit individual participants?</th>
<th>Does it exploit communities?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trials that use a placebo control, especially where such trials would be considered unethical in developed countries</td>
<td><em>Wertheimer:</em> Such research exploits participants only if the net benefit to participants (especially those randomized to placebo) falls below “market value.” It is possible that benefits might fall above that threshold for participants randomized to active treatment, but below it for participants randomized to placebo.</td>
<td><em>Wertheimer:</em> the community would only be exploited if the net benefit to the community falls below market value (accounting for the degree to which the community is a party to the transaction). A Wertheimerian analysis would not have to consider whether individual community members were treated fairly in answering this question.</td>
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<tr>
<td></td>
<td><em>Sample:</em> Randomizing an individual to a placebo arm could be degrading in itself, especially if that individual is compelled to participate because of past injustices and if the research as a whole is not sufficiently attentive to his or her well-being.</td>
<td><em>Sample:</em> The trial could be degrading to the community if its members degraded. Such a trial would also be especially disrespectful to the community if it is not responsive to local health needs. (See below.)</td>
</tr>
<tr>
<td>Research that does not provide fair benefits to the respective party, in the form of a successfully tested product or some other means.</td>
<td><em>Wertheimer:</em> This is where Wertheimer’s theory applies most cleanly. He defines fair (or at least non-exploitative) benefits as whatever the hypothetical market approach yields. Such research would be exploitative if the benefits to participants fall below that value.</td>
<td><em>Wertheimer:</em> Communities could be exploited if benefits to the community (insofar as it is a party to the transaction) fall below market value.</td>
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<td></td>
<td><em>Sample:</em> Sample denies that providing benefits that fall below market value constitutes exploitation. Her notion of fair benefits depends instead on what is necessary for participant’s well-being and flourishing. Research that is not sufficient</td>
<td><em>Sample:</em> Sample’s notion of degradation does not depend on the community being party to the transaction. In the case of the community attentiveness to flourishing and well being is synonymous with responsiveness (below).</td>
</tr>
<tr>
<td>Research that is not responsive to local health needs.</td>
<td>Wertheimer: Wertheimer’s theory does not apply here; if the individual participant is sufficiently compensated, there is no need to take the community into account.</td>
<td></td>
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<tr>
<td>Sample: Such research could be seen as disrespectful to (and therefore exploitative of) individuals in that it treats them as purely as individual and neglects their being part of a community.</td>
<td>Sample: non-representative research exploits the community if it is not sufficiently attentive to the community’s well-being and flourishing. This appears synonymous with responsiveness.</td>
<td></td>
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</table>

**APPENDIX II: THE MANDATE OF RECS ACCORDING TO SELECTED CODES OF ETHICS**

<table>
<thead>
<tr>
<th>Document</th>
<th>Passages Relating to the Mandate, Roles and Responsibilities of RECs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Declaration of Helsinki</td>
<td>Article 13: “This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee…”</td>
</tr>
<tr>
<td></td>
<td><em>No specific guidance with regards to independent review of international research.</em></td>
</tr>
</tbody>
</table>
| CIOMS Guideline     | Commentary on Guideline 2: “Ethical Review: The ethical review committee is responsible for safeguarding the rights, safety and well-being of research subjects… It should consider whether any known or possible risks to the subjects are justified by the expected benefits, direct or indirect, and whether the proposed research methods will minimize harm and maximize benefit.”
|                     | “The basic responsibilities of ethical review committees are… to ensure that all other ethical concerns arising from a protocol are satisfactorily resolved both in principle and in practice.”
<p>|                     | <em>With regards to international research:</em> Guideline 3: “Committees in the host country have a special responsibility to determine whether the objectives of the research are responsive to the health needs and priorities of that country.”                                                                                                                                                                                                                       |
| UNAIDS Guideline    | Does not deal with this explicitly.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |</p>
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<th>Text</th>
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| TCPS                                       | Commentary on Article 1.1: “The REB is established to help ensure that ethical principles are applied to research involving human subjects…”  
Article 1.2: “The institution in which research involving human subjects is carried out shall mandate the REB to approve, reject, propose modifications to, or terminate any proposed or ongoing research involving human subjects that is conducted within, or by members of, the institution, using the considerations set forth in this policy as the minimum standard.”  
*With regards to international research:* Article 1.14: “Research to be performed outside the jurisdiction or country of the institution which employs the researcher shall undergo prospective ethics review both (a) by the REB within the researcher’s institution; and (b) by the REB, where such exists, with the legal responsibility and equivalent ethical and procedural safeguards in the country or jurisdiction where the research is to be done.” |
| 45 CFR 46 (The Common Rule)                | 46.109 IRB Review of research. “An IRB shall review and have the authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy.  
46.111 Criteria for IRB approval of research. “(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied: (1) Risks to subjects are minimized… (2) Risks to subjects are reasonable in relation to anticipated benefits… The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility. (3) Selection of subjects is equitable… (4) Informed consent will be sought from each prospective subject…”  

*No specific guidance with regards to independent review of international research.* |
| ICH-GCP Guideline                          | Article 3.1.1: “The IRB/REC should safeguard the rights, safety and well-being of all trial subjects. Special attention should be paid to trials that may include vulnerable subjects.”  

*No specific guidance with regards to independent review of international research.* |