Human Guinea-Pigs Wanted!

An Evaluation on Exploitation in HIV Clinical Trials:
Case Cambodia and High-Risk Women

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ABSTRACT

The aim of the study is to evaluate the risk of “high-risk women” being exploited as research participants in HIV clinical trials, conducted in resource-poor settings. The study includes a case-study with a particular focus on the contextual circumstances of Cambodia, and adult female sex-workers (and injecting drug users). A qualitative research approach has been applied, which involves a literature study, including an empirical, and a theoretical research structure. The theoretical part of the study entails the Wertheimerian concept of exploitation, on the subject of clinical research, whereas the empirical study consists of a context analysis regarding Cambodian high-risk women, and the risk of exploitation. Additionally, a risk assessment tool, including four risk indicators, has been used to facilitate the estimation of the level of risk of exploitation – weather the risk of exploitation is of great concern, or not.

The research result reveals that there is a big possibility that pharmaceutical companies might find Cambodian high-risk women as an interesting target group for HIV research purposes. However, enrolling high-risk women in HIV clinical trials necessitate careful consideration in view of their vulnerability as research participants. Cambodian high-risk women are among the most stigmatized and discriminated population in Cambodia, they are often denied health care, and their socio-economical status is low. Taking part in research as clinical participants might therefore be a desperate act for receiving a possible compensation, such as free health care or a certain amount of money. The benefits which high-risk women might be compensated with as potential research participants are, on the other hand, measured as unfair, in comparison to the possible side effects and other related risks a trial might engage, but also in contrast to the huge profits which pharmaceutical companies are more likely to gain from the same transaction. To avoid the possibility of high-risk women’s unfortunate circumstances being taking advantage of, require that clinical trials are evaluated and that ethical standards are respected. However, the efficiency and the reliability of the so-called control mechanism for research are questioned. Consequently, it is estimated that Cambodian high-risk women are at great risk of being exploited as research participants in HIV trials.

Keywords: research ethics: exploitation: HIV trials: high-risk women: Cambodia
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<th>Acronym</th>
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<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
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<td>ART</td>
<td>Antiretroviral Treatment</td>
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<td>Antiretroviral</td>
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<td>BSS</td>
<td>Behavioral Surveillance Survey</td>
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<td>CIOMS</td>
<td>The Council for International Organizations of Medical Sciences</td>
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<td>DoH</td>
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<td>EDCTP</td>
<td>The European and Developing Countries Clinical Trials Partnership</td>
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<td>Female Sex Workers</td>
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<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>ICESCR</td>
<td>The Committee on Economic, Social and Cultural Rights</td>
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<td>IDU</td>
<td>People who Inject Drugs</td>
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<td>MARP</td>
<td>Most at Risk Populations</td>
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<td>MDGs</td>
<td>The United Nations Millennium Development Goals</td>
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<td>MoH</td>
<td>The Ministry of Health</td>
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<td>MSM</td>
<td>Men who have sex with men</td>
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<td>MWVA</td>
<td>The Ministry of Women’s and Veterans Affairs</td>
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<td>NCHADS</td>
<td>The National Centre for HIV/AIDS, Dermatology and Sexually Transmitted Infections Phnom Penh, Cambodia</td>
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<td>NGO</td>
<td>Non-Governmental Organization</td>
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<td>NIH</td>
<td>The National Institutes of Health</td>
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<td>PLHA</td>
<td>People Living with HIV/AIDS</td>
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<td>PrEP</td>
<td>Pre-exposure Prophylaxis</td>
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<td>UCSF</td>
<td>The University of California, San Francisco, CA, USA</td>
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<td>UNAIDS</td>
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<td>UNDP</td>
<td>United Nations Development Programme</td>
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<td>UNSW</td>
<td>The University of New South Wales, Sydney, Australia</td>
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<td>USD</td>
<td>U.S. Dollar</td>
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<td>WHO</td>
<td>The World Health Organization</td>
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<td>WNU</td>
<td>Women’s Network for Unity</td>
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ESSAY OUTLINE

The first part of the report begins by describing the necessity of HIV medical treatment, and HIV prevention tool to control the epidemic, which includes vaccination treatment, and the significance of medical research. The report continues by defining a high-risk population, and by discussing the ethical concern of enrolling vulnerable research participants in HIV clinical trials. The aim of the study is also presented, as well as the research question, followed by some brief information about the Cambodian tenofovir trial. Chapter two presents an accurate description of the methodological approach of the study, including, among other, data collection and analytical tools. Chapter three represents the theoretical part of the report, which consists of a concept discussion on the subject of exploitation in clinical research, and a short presentation of research procedures related to clinical trial activities. Chapter four demonstrates a risk assessment tool that will be applied on the empirical part of the study. The empirical part of the report (chapter five) includes a context analysis with particular focus on Cambodian high-risk women, and the risk of exploitation in HIV clinical research. The report finally ends with some concluding remarks in chapter six.
1. BACKGROUND

HIV stands for Human Immunodeficiency Virus. It affects the white blood cell that consequently reduces the immunity in the human body which gradually causes AIDS (Acquired Immune Deficiency Syndrome), including a group of health problems and infections, known as opportunistic infections such as pneumonia or chronic diarrhea. Unlike AIDS, the HIV virus can be avoided, yet it cannot be cured. It is almost three decades since AIDS began ringing global alarm bells; still no vaccine is in sight. However, some significant progress has been seen and intensive efforts are continuing to increase access to HIV prevention tools. HIV/AIDS prevention, treatment and care include a diversity of HIV equipments such as e.g. HIV diagnostics, condoms, and HIV-drugs. To improve the global access of these services, an increased and consistent production of antiretroviral medication might be seen as one of the key methods (UNAIDS 2008; WHO 2009a). Enable to respond to AIDS in a long term perspective, depends on the progress in HIV research, requiring several aspects including e.g. the understanding of the determinants of HIV transmission; developing effective therapies to treat HIV-related diseases; and evaluating the effectiveness of a variety of approaches to prevent new infections. HIV vaccine is considered as the best hope for ending the epidemic, but developing one involves various challenges, in relation to the rapid mutation of the HIV virus. Scientists might get promising outcomes in laboratory testing and from studying animals, yet the only way to discover whether e.g. a biomedical HIV prevention approach is effective, if an intervention has side effects, or implicates for drug resistance, is to try the strategy out on humans. A number of 50 vaccine trials are currently being in progress or scheduled, in a verified amount of more than 30 countries, around the world. The advanced research is to a large extent being carried out in Asia and Africa, where the majority of the new HIV infections are taking place. Other prevention strategies undergoing human testing include among other; vaginal microbicides such as creams, gels, or rings that release anti-HIV microbicide over time; and pre-exposure prophylaxis (PrEP) that consists of anti-retroviral medications, taken as a single drug or as a combination, on a daily basis, with the aim of protecting people from obtaining HIV (UNAIDS 2007; UNAIDS 2010f).
1.1. Introduction

Pharmaceutical companies have a major influence on individuals’ basic human right to enjoy the highest attainable standard of physical and mental health (Article 12.1 of the International Covenant on Economic, Social and Cultural Rights), and the right to a standard of living adequate for the health and well-being of himself and of his family, including among other medical care (Article 25.1 of the Universal Declaration of Human Rights). In 2000, the Committee on Economic, Social and Cultural Rights (ICESC) recognized that the private sector has responsibilities in relation to the right to health. The committee also concluded that the right to the highest attainable standard of health includes both entitlements such as access to fundamental drugs, and freedoms from e.g. non-consensual medical treatment and experimentation. Clinical trials are for that reason subject to strict regulations and have to be pre-approved by authorities and ethical committees (CESCR 2000; Sjödin 2008; WHO 1995). The Declaration of Helsinki (DoH) issued by the World Medical Association, was adopted in 1964 and has been updated since, most recently in 2008. The declaration is the fundamental document on ethics in human studies on the international level to guarantee the reliability of clinical research and to declare that the rights, safety, and well-being of research subjects are protected. Further significant approaches have been established by among other the Council for International Organizations of Medical Sciences (CIOMS). In 1993, CIOMS initiated highly preventive international ethical guidelines for biomedical research involving human subjects, requiring among other that control arms should not fall below the world’s best-known-treatment (CESCR 2000; Sjödin 2008; WHO 1995; CIOMS 2002).

1.1.1. High-Risk Population

Enable to collect scientifically valid research involve that HIV trials be carried out in locations where there are adequately high numbers of HIV infected people; where people are exposed to HIV and therefore at high risk of getting infected by HIV; and furthermore, where efficient interventions may have the greatest outcome. This type of locations often involves the most socially vulnerable areas of society. HIV generally gets its first grip among exposed groups in urban areas, and spreads to the rural areas as the epidemic becomes generalized (UNAIDS 2007; UNAIDS 2010abc).
People’s exposure to HIV infection is increased by a range of social and economic aspects, including stigma and discrimination, poverty and lack of HIV awareness and access to education and health services, among other. Rural population in low- and middle-income countries tends to be particularly deprived in terms of social services, and millions worldwide have no access to HIV prevention, health care or support. HIV infections are in most cases sexually transmitted. Environments in which people have multiple sex partners are particularly contributing to the spread of the virus, whereas sex workers and their clients often become the first victims of the epidemic (UNAIDS 2007; UNAIDS 2010abc).

The HIV epidemic has had a severe effect on human development, in many parts of the world, hindering the process of achieving the United Nations Millennium Development Goals (MDGs), mainly those related to poverty reduction, gender equality, and improving the health of mothers. This, in turn, has left numerous of women at even higher risk of HIV exposure. It is estimated that almost half of the adults living with HIV today are women. The number of infected women and girls has increased over the past two years particularly in Eastern Europe, Latin America, and Asia. Lack of education or economical opportunities often result in women becoming reliant on men in their relationships. In locations where women are not allowed to own property, or where they lack legal protections, dependence within their families is even greater. Many women who do not have any economical support are forced to find an optional way of income by e.g. selling sex enable to support themselves and their children. Women's economical and social dependence on men often restrict women's ability to refuse sex or to negotiate the use of condoms, which consequently increases the risk of HIV transmission. HIV infected women, and those whose partners have died of AIDS are frequently discriminated or neglected, and in some contexts, less likely of receiving appropriate health care (UNAIDS 2007; UNAIDS 2010de).
1.2. Ethical Concern

In recent years, there has been criticism from among other human rights activist regarding suspected faults in the practice of clinical trials, involving human participants. Debates have become particularly intense over suggestions regarding clinical trials in low- and middle-income countries, to test new drugs and procedures in highly impoverished communities. Efforts to decide when it is acceptable to carry out clinical research have been noticeably influenced by the past; by how it has been conducted or in fact misconducted. Even if unethical trials have been reported from both high-income countries and low- and middle-income countries, some countries appear to have a more failing regulatory system than others, leading to more serious outcomes. In the broad context of research, exceptions regarding requirements of equipoise and standards of care are occasionally acceptable for participants whom are agreeable to take further risks on altruistic basis. Such exceptions are, on the other hand, resisted for research on vulnerable populations, such as acutely ill and deeply impoverished people. The policy is found as a preventive measure enable to guard against the risk of exploitation (UNAIDS 2007; Hawkins and Emanuel 2008, p.13).

1.3. Research Problem

Participating as a medical volunteer in a clinical trial in hope for health care or financial compensation, could be tempting among high-risk populations in resource-poor settings, where access to effective health treatment might be insufficient, or non affordable. A problematic aspect is the probability that pharmaceutical companies might find high-risk women as an attractive target for exploitation; taking unfair advantage of vulnerable women’s circumstances, enable to maximize profit and gain scientific knowledge. Consequently, a high-risk population may not only be at risk of receiving HIV-infection, but also at risk of being exploited as research participants.

1.4. Purpose

The intention of the study is to evaluate the risk of “high-risk women” being exploited as research participants in HIV clinical research, conducted in resource-poor settings.
1.5. Research Question

- Are Cambodian “high-risk women” at great risk of being exploited as research participants in HIV clinical trials?

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“Exploitation” refers to the Wertheimerian concept of exploitation. Further details regarding the concept of exploitation is presented in chapter three. The research question indicates that the female high-risk populations of Cambodia are at risk of being exploited as research participants in HIV trials. But whether the risk of exploitation is of great concern have not, on the other hand, been clarified. A risk assessment tool will, therefore, be applied enable to estimate the level of risk, of exploitation.

Both an empirical and a theoretical research framework will be used, enable to answer the research question. The theoretical part, involves the concept of exploitation with particular consideration on the moral concerns associated to exploitation in clinical research. The vulnerability of research participants’ in addition to the possible risks and benefits related to clinical research, are analyzed and discussed. The empirical part of the research approach consists of a contextual analysis, which identifies and evaluates the possible risks and benefits of enrolling high-risk women in HIV clinical trials, along with high-risk women’s vulnerability as research participants. The context analysis continues by evaluating pharmaceutical companies’ possible interests of enrolling Cambodian high-risk women in HIV trials; whether there are any existing community standards that are adequate enable to evaluate research applications; as well as other possible obstacles which could increase the risk of high-risk women being exploited as research participants in HIV clinical trials. The research findings are analyzed by clarifying patterns and connections to the theoretical part of the report, enable to answer the research question and to attain the aim of the study.
1.6. Delimitation

The study will focus on high-risk women and HIV-trials in Cambodia

Cambodia is located in South East Asia, bordering Thailand to its west, and Laos and Vietnam to its east. Cambodia has a population of over 14 million people, and is described as one of the most rapidly growing HIV/AIDS epidemics in the world, concentrated particularly among the high-risk groups of the female population (WHO 2001; CIA 2009). I therefore find it very likely that pharmaceutical companies might view Cambodia as a significant location to carry out HIV research, and that Cambodian high-risk group women could be identified as potential research participants. An additional reason why I find Cambodia as an appropriate target for evaluation on the topic of exploitation in HIV research, is because of the controversial and highly debated “tenofovir trial”.

1.6.1. The Tenofovir Trial

The Cambodian trial (also known as the tenofovir trial) was planned in Cambodia, on August 13, 2004, in collaboration between the University of California, San Francisco, CA, USA (UCSF); the University of New South Wales, Sydney, Australia (UNSW); and the National Centre for HIV/AIDS, Dermatology and Sexually Transmitted Infections, Phnom Penh, Cambodia (NCHADS). The funding sponsors were among other a US-based research organization that had received a grant from the Bill and Melinda Gate Foundation. The study was supposed to include a randomized trial that recruited 960 HIV-negative adult female sex-workers. The aim of the research was to determine the safety and effectiveness of daily oral tenofovir disoproxil fumarate, in preventing the sexual transmission of HIV infection. However, the trial was cancelled in 2004 by Cambodian authorities, and the study was never completed. Instead, researchers were blamed for planning to engage in practices that were conflicting with the standards of research ethics, and that the trial was mainly motivated by the commercial interests of a pharmaceutical company. It should be recognized that there are different opinions about the tenofovir trial (Shafer & Saphann, et al., 2005; Hammer & Lundstrom 2005).
2. METHOD

A qualitative research approach will be used for the purpose of this study. There is a wide diversity of methods that are common in qualitative research. A qualitative research approach does not, on the other hand, engage measurement or statistical procedures. Instead, qualitative research usually includes methods such as observations, interviews, and case studies. In contrast to quantitative methods – qualitative data collections consist of smaller number of people and cases, which in turn, facilitate the evaluator to study selected issues in depth and in detail, by for example carefully describing program situations, people, or interactions. Case studies are regularly measured as valuable when one needs to evaluate some particular problem or situation in great depth. A “case” might be a person, a critical occurrence, or perhaps a community. However, regardless of the unit of the analysis, the intention of a qualitative case study is to illustrate that unit in depth, in detail, in context, and holistically. A holistic approach, assumes that a description and understanding of a program’s social, political, or economical context, is important for overall understanding of that program. A case study, with a holistic approach, will for example be applied in this study, in order to understand the context of Cambodia, and Cambodian high-risk women (Patton 1987, p.9, 17, 19).

2.1. Cambodian “High-Risk Women”

According to available statistics from 2006, 52 percent of infected people in Cambodia were female. However, due to existing gender inequities in Cambodia, sexual transmission continues to increase. In 2003, the Ministry of Women’s and Veterans Affairs (MWVA), recognized that Cambodian customs made it inappropriate for women to be sexually aware or to discuss safe sex or condom use, limiting women’s ability to control their own bodies, and increasing their exposure to HIV. Domestic violence was another explanation why women were considered as more exposed to HIV and AIDS (Cambodian Parliament 2010; NAA 2008). There are three central most at risk populations (MARP) in Cambodia: (1) people who inject drugs (IDU); (2) men who have sex with men (MSM); and (3) female sex workers (FSW). However, as a consequence of insufficient data, no one really knows how many people each category of the MARP involves, or what the actual HIV rate among them is (Cambodian Parliament 2010).
In addition, the 2007 Behavioral Surveillance Survey (BSS) found that the Cambodian sex industry is moving from brothel-based sex workers to non brothel-based settings including e.g. “beer girls” and women working in Karaoke and massage parlors. This transformation has raised concern, making targeted prevention programs even more complex. Further concern are related to the increasing use of illicit drugs in Cambodia, and the plausible connection between such drug use with enhanced sexual transmitted infections, including HIV. “Yama” (methamphetamine) appears to be the most widely used illicit drug, with regard to HIV transmission, and has been found among the most at risk populations in Cambodia, including female sex workers in Phnom Penh (USAID 2006; Korsang 2010).

2.1.1. The Target Group

The target group for this study involves Cambodian women who engage in behaviors which put them at a higher risk of becoming HIV infected. In view of the context of Cambodia, the high-risk women include: female sex workers, as well as female sex workers whom inject illicit drugs.

- “Sex work” (or commercial sex work) refer to any sex act on account of which anything of worth is given to or received by any person (U.S. Department of State 2007).
- The target group is restricted to only include adult women (age 18 and above, in accordance to the UN Convention on the Rights of the Child (1989) Part 1, Article 1).
- Illicit drugs refers to “Yama” (methamphetamine)
2.2. Data Collection

According to Michael Quinn Patton, various strategies of data collection should be used enable to increase the validity and reliability of research findings, as well as to give a deeper understanding regarding a specific topic (Patton 1987, p.16, 60). A field study in Cambodia might for example have given the opportunity to use further methodological approaches such as observations or interviews with information-rich cases. An observation could for example have involved the physical location where clinical trials might have been conducted, or where individuals where recruited to participate in research. Such observation could have revealed more about the indoor- and the outdoor environment, considering e.g. the standard of care, personnel service, and location; information which could be considered as relevant when examining a clinical trial process in accordance to international ethical standards. Whereas, the information-rich cases might have included research participants, or potential research participants, personnel from a clinical team, female sex workers (including injecting drug users) or an organization representative that works with high-risk women. By interviewing such “cases” one could have gotten the opportunity of finding out more about e.g. the individuals motivations for participating in HIV clinical trials; how individuals identified their role as research participants; and their personal thoughts and experiences regarding exploitation in research. The informants could also have provided details regarding the inclusion criteria, informed consent, possible health benefits, paid compensations, insurance, and follow-ups; aspects which are of great value when evaluating the risk/benefit ratio of a trial. Considering that the aim of this study is to evaluate the risk of exploitation, and not to conclude whether a particular trial is exploitative; a field study would therefore have required a collection of a broader range with information-rich cases with no necessary association to a certain clinical trial. A further rather important issue regards the Law on Suppression of Human Trafficking and Sexual Exploitation, and its negative impact on female sex workers and anyone that has any particular association with sex work, including organizations for sex workers (more details regarding the law is discussed in chapter 5.2). Consequently, in view of the controversy of the subject being evaluated, and the vulnerability of the target group, a number of informants might not have been willing to take part in the study. Because of limited time and resources, a field-study was not to be considered as an option. Instead, the thesis is based simply on a literature-study, including an empirical, and a conceptual (theoretical) research framework.
A literature study is an effective approach enables to evaluate selected documents on a research topic. A literature study provides a background which reflects on aspects that are considered relevant to the research question being posed. It might include aspects such as clinical practice, or perhaps the theoretical background, as regards to e.g. the concept of exploitation. In addition, a theoretical (conceptual) research framework is used in the evaluation to present the definition of “exploitation” that will be applied in this study. The definition involves Alan Wertheimer’s view on exploitation, also referred to as the so-called “Wertheimeran concept of exploitation”. Alan Wertheimer, Professor of Political Science, is the author of Coercion and Exploitation (Princeton University Press, 1996), and numerous of articles and chapters in books regarding the topic of among other, exploitation and research ethics. According to Wertheimer’s concept of exploitation – “exploitation” is a micro-level concern which focuses on the parties who interact. Considering that the aim of the study focus on a particular target group, on whether they are at risk of being exploited in a transaction, and not whether other people unrelated to the possible interaction are at risk of being exploited, is a significant reason why I have determined to use the Wertheimerian view on exploitation, in this particular evaluation. In addition, the theoretical framework also entails moral worries that are associated to the topic of exploitation in clinical research. Theoretical (conceptual) frameworks could be described as some sort of transitional theory that seek to connect to all parts of the assessment, such as literature study, purpose, and analysis. Theoretical frameworks functions like maps that provide reliability to the empirical analysis. Empirical research frameworks, on the other hand, are an approach for attaining information, and are generally used in order to answer a specific question, or to test a hypothesis. The empirical framework applied in this particular evaluation includes a case study; a contextual analysis with a focus on Cambodia, and Cambodian high-risk women (Hart 1998; Botha 1989; Hawkins & Emanuel 2008, p.293-295).

It should be pointed out that efforts have been made in hope to get in touch with relevant organizations that are active in Cambodia. They were contacted via e-mail with a short presentation regarding the aim of the study, and the research question, along with an invitation to take part in an interview via telephone or the internet. Yet, no respond have been made. The reason why they did not respond is questioned, and one could only speculate whether it possibly have something to do with the aim of the study or the research question.
2.2.1. Research Material

Carefully selected sources of secondary material will be used in the research. The research material has been collected via library and the Internet (e.g. Google Scholar, Pub Med, Medline, nongovernmental organizations and governmental websites). Scientific publications usually involve a higher quality and validity, in comparison with information provided by e.g. nongovernmental organizations, why the reliability of collected information is being taken into consideration.

International ethical guidelines and regulations, scientific reports, and official documents from public authorities and organizations, will be applied enable to present the current situation regarding HIV research; research procedures within HIV trials, medical treatments, product safety, and pharmaceutical companies’ responsibility towards research volunteers. Theoretical literature on different perspectives on research ethics and exploitation, scientific evaluations on previously conducted trials, and ethical guidelines, will be used in the concept discussion; regarding moral concerns related to exploitation in clinical research. The research material applied in the theoretical part of the study (the concept discussion) will help to distinguish the risk indicators (described in chapter four) that will be used in the research evaluation. Further reports includes governmental and nongovernmental reports regarding female sex-workers, their socio-economical status, access to medical health care services, along with reports on human rights abuses, and statistical findings on the Cambodian public health situation. These findings will be useful enable to explain high-risk women’s current contextual circumstances, their likelihood of participating in HIV trials, their vulnerability as research participants, and the risk of high-risk women being exploited in HIV trials.

Reports regarding pharmaceutical companies’ activities and research collaborations will help to reveal further details regarding ongoing trials in Cambodia. The findings might expose pharmaceutical companies’ possible interests of enrolling high-risk women in HIV clinical trials, and may therefore be applicable when evaluating the risk of exploitation. Further relevant research materials include community standards, and regulations that are related to high-risk women’s contextual circumstances, and the risk of exploitation. Scientific evaluations on previously conducted trials such as the Cambodian tenofovir trial can also be useful enable to distinguish certain ethical aspects and risk factors, which can be applied in the context analysis.
2.3. Analysis Approach

The evaluation approach of the study includes a combination between an inductive and deductive design. “Inductive” analysis means that the patterns, topics, and categories of analysis emerge out from the data, rather than being determined prior to data collection and analysis. An evaluation approach is inductive to the point that the evaluator tries to understand the existing program patterns, without inflicting pre-existing expectations on the program-setting. In contrast to a goal-free inductive approach, a “deductive” approach usually evaluates relative achievement of predetermined, specific, goals. These two approaches are, however, frequently combined in research evaluations. An evaluator might for example start by using an inductive approach, to find out what the significant questions and variables are; followed by a deductive design to confirm the exploratory findings; to finally end with an inductive analysis, to look for opposing hypotheses and unexpected or measurable factors (Patton 1987, p.15-16,150). Furthermore, a so-called “risk assessment tool” have been developed, making it possible to estimate the level of risk of exploitation. The risk assessment tool is necessary enable to answer the research question and to accomplish the aim of the study. More details regarding the assessment tool are presented in chapter four.

2.3.1. Concerns about the Methodological Approach

The fact that science places great value on objectivity, might explain why concerns on the subject of qualitative methods often involves the subjectivity of the evaluator. The conclusions drawn through the interpretation of the results of data analysis ought to be based on the facts of the findings derived from data and not on our own personal or emotional values. A reasonable aim is for the researcher to admit their own opinions and to operate in a value-free way as possible, enable to stay objective to the outcome of the research. However, philosophers of science usually doubt the likelihood of any person, or any methodological approach being truly “objective”. A similar concern is about getting hold of the truth. However, search for “truth” implies a single correct answer, whereas qualitative methods presuppose multiple perspectives, and therefore, multiple “truths” depending on diverse opinions. For instance, by using another concept of “exploitation” as a replacement for the “Wetheimerian concept of exploitation” would almost certainly provide a different outcome in comparison to the result presented in this particular report (Patton 1987, p.166).
Another rather typical concern is the small sample sizes that are usually involved in qualitative methods and the impossibility of generalizing. A low amount of cases cannot be representative to a larger population. However, as already been mentioned, the strength by using a smaller sample size, is the possibility to study a carefully selected issue in detail (Patton 1987, p.9, 167). Consequently, with particular consideration to the limited data used in this study, the final result will not be representative to all high-risk women in Cambodia, but it might, on the other hand, give a more in depth understanding of the issue – the risk of Cambodian high-risk women being exploited as research participants in HIV clinical trials.

2.4. Previous Studies

Previous research is available on the concept of exploitation in clinical research, and ethical concerns related to research conducted in resource-poor settings. The official documents are published by researchers, governments, and nongovernmental organizations (NGO), among other. However, reports concerning human rights issues in Cambodia are generally provided by NGOs. Statistics on specific topics, regarding high-risk populations or estimated HIV prevalence in Cambodia are in many cases missing. Besides the tenofovir trial, no study could be found which included interviews with clinical participants, high-risk women, or other vulnerable groups in Cambodia, regarding the topic of clinical research, and exploitation.
3. EXPLOITATION IN CLINICAL RESEARCH

In the most general sense, “to exploit” simply means to use something or someone to advantage. However, bearing in mind that not all “use” of people is morally problematic, with the fact that the term “exploitation” itself can be used in morally loaded and morally neutral ways – “exploitation” might be considered as rather unclear. For example, in the claim that (A) exploited the hill to get a good view of the ocean, or in a case where a weight lifter exploits his/her muscles to lift weights - “exploitation” is used in a non-moral sense (Hawkins & Emanuel 2008, p.13, 44). What separates exploitation as a particular form of injustice might be considered as somewhat controversial. But, what is considered as relevant in the subject of wrongful exploitation, is the relation between the parties that are affected by a certain situation, which in many cases is closely connected to unfair social and economical circumstances. The general claim of exploitation is that: (A) wrongfully exploits (B) when (A) takes unfair advantage of (B) (ibid. p. 65, 67).

According to Alan Wertheimer, “taking unfair advantage” could actually be understood in two ways. First, it might refer to the outcomes of an unfair exploitative transaction, considering the benefit to (A) and the effect on (B). For instance, the benefit to (A) might be unfair because it is wrong for (A) to benefit at all from his act, by e.g. harming (B); or because (A)’s benefit is unfair in comparison to the benefit to (B). Second, to claim that (A) takes unfair advantage of (B) could also involve some sort of failing in the course of action which might lead to unfair consequences, for example that (A) fails to provide (B) with relevant information, or that (A) coerces (B) into giving consent (ibid. p.68- 69).

3.1. “Unfair Advantage”

Picture an unemployed person in search for work, who meets a potential employer that offers him/her a new job. The new job offer involves no health benefits, unsafe working environment, for less than a minimal wage. Fully aware of the unfair conditions the person still freely chooses to accept the job offer, thinking that it might be the best choice available at the time, in view of his/her unfortunate life situation – “a bad work environment is better than no work at all”. What is pointed out as morally problematic in this case, concerns the employer who is taking unfair advantage of a person’s unfair conditions (Agrawal 2003).
Even though the case might be considered as a typical illustration of wrongful exploitation, Wertheimer finds it important to differentiate between the claim that (A) is “taking unfair advantage” of (B) and the claim that (A) is “taking advantage” of (B)’s unfair conditions. Wertheimer explains that it is possible for (A) to take advantage of unfairness to (B) without actually taking unfair advantage of (B). For instance, imagine another case where (A) offers to amputate (B)’s leg for a fair fee. Since (B) will die unless she consents to the amputation, (B) authorizes (A) to carry out the surgery. Although (B) has no reasonable alternative to agree to (A)’s suggestion, (A) does not exploit (B) because a transaction is exploitative only if the distribution of the benefits is unfair. And, even if (B)’s current circumstances is unjust and not simply unfortunate, it does not pursue that the transaction between (A) and (B) is exploitative (Hawkins & Emanuel 2008, p.71). In addition, Wertheimer argues that (A) cannot take unfair advantage of (B) unless (A) gets some advantage from the transaction with (B). So, if (A) does not benefit from the transaction, (A) does not exploit (B). For instance, let say that (A) oppresses (B) when (A) deprives (B) of freedoms or opportunities to which (B) is entitled. If (A) benefit from the oppressive relationship, then (A) might both oppress and exploit (B). However, if (A) does not benefit from the oppression, in that case, the oppression is wrong, but not exploitative. It should also be pointed out that (A) might actually exploit (B) while trying to serve entirely generous ends. It might, for example, involve a clinical trial in which the medical researchers exploit the participants for the benefit of others (ibid. p.69-70).

According to the Wertheimerian view of exploitation – exploitation is about the fairness of an individual exchange, and is therefore described as a micro-level concern. There is no doubt that larger social injustice of macro-level distributions of background rights and resources forms our existence and can influence exploitation. However, the actual experience of exploitation occurs at micro-level interactions, between for example researchers and the population of the community who takes part in the research. Therefore, determinations of exploitation, in accordance to the Wertheimerian concept of exploitation, ought to focus on the level of benefits provided to the parties who interact, and not the kind of benefits people unrelated to the interaction receives (ibid. p.293-295).

It has already been clarified that (A) has to benefit from the transaction with (B) enable to exploit (B). But, let us say that both (A) and (B) benefit from the same transaction, a so-called “mutually advantageous transaction” – So, how do we determine whether a mutually advantageous transaction is unfair?
For instance, (A), who is “wealthy”, offers to pay (B) USD25000 for one of his kidneys for purposes of transplantation. (B), who on the other hand is “poor”, agrees in order to better provide for her family. It is obvious that the transaction is beneficial to both (A) and (B), but it does not signify that the transaction between (A) and (B) is exploitative, unless we can verify that the distribution of the benefit is unfair. Some might argue that a transaction is unfair when the goods exchanged are “incommensurable” (not possible to measure). But according to Wertheimer, it is not apparent whether and when goods are incommensurable. It is usually argued that an exchange is unfair when the exploitee receives too little. But, if we cannot compare what the parties gain - how is it possible to claim that the assumed exploitee receives too little, and that the exchange, for that reason, is unfair? Second, imagine that it is possible to compare the gains of the parties – then how should we measure their relative gains? For instance, it is frequently suggested that a transaction is exploitative when (A) gains much more than (B). But, if a doctor overcharges for a lifesaving surgery that only he can carry out, the patient still gains much more than the exploiter. The doctor gains some money; while the patient gets her life back. This example indicates that we cannot evaluate the fairness of a transaction merely by comparing how much value the parties get from the transaction (Hawkins & Emanuel 2008, p.65, 72-74).

Wertheimer suggests that we, to a certain extent, should evaluate the fairness of their gains against a so-called “normative standard”, as to how much the parties ought to gain. But, until such type of standard have been developed, Wertheimer basically assume that some mutually advantageous transactions are unfair, by reference that (A) exploits (B), when (A) gains more than (A) should; or (B) gains less than (B) should, from the transaction (ibid. p.65, 72-74).

In addition, it should be pointed out that exploitation, in accordance to the Wertheimerian conception of exploitation – is not whether or not the level of benefits is equally distributed, but about the fairness of the level of benefits. An unequal distribution of the benefits might for example be measured as fair, if there are differences in the burdens and contributions of each party (ibid. p.294).
3.1.1. “Unfair Transaction”

Wertheimer also believes that a morally failing outcome is required in order to uphold an exploitation claim. However, since there are significant moral dissimilarities among diverse cases of exploitation, such as e.g. consensual- or non-consensual exploitation, Wertheimer finds it crucial to look upon them as faults in consent as well. With “consensual exploitation” Wertheimer refers to cases where e.g. the exploited party has given voluntary and appropriately informed consent to the transaction, or where the transaction is mutually advantageous. Cases, in which the exploited have not been given his or her approval in taking part in the transaction, are referred to as “non-consensual exploitation”. There are several cases in which consent fails – yet, there is no question of exploitation. For instance, a clinical trial, carried out by (A) in which participants (B) receive an experimental treatment, whereas the researchers ignore to provide adequate information, is very likely to be criticized as unethical (considering the fact that informed consent is more or less generally accepted as an essential requirement of ethical research). While such clinical trials might be judged as unethical, the researchers are not, on the other hand, automatically claimed to be exploiting the participants. So, even though the truth of an exploitation claim does not assume any failing in consent, the moral incentive of an exploitation claim may revolve on whether the exploitation is consensual or non-consensual (Hawkins & Emanuel 2008, p.7, 69, 74-77, 206)

A general view is, for example, that some of the most difficult moral worries start, rather than end, with voluntary agreement. Coercion, manipulation and fraud, undermine the voluntariness of agreement and are therefore considered as immoral or wrong, whereas agreements that are based on a voluntarily approval of e.g. possible burdens and benefits may be considered as morally acceptable. The voluntariness of certain transactions might consequently not seem innocent of wrongdoing. In view of that, there might be reason to prohibit non-consensual exploitation, whereas consensual exploitation might be permissible. In addition, Wertheimer clarifies that it is important to verify whether a possible exploitative transaction is sufficiently consensual, or not. For example, the case in which (B) agrees to amputation, demonstrates the simple fact that (B) might have no acceptable option to accepting (A)’s offer, but does not, on the other hand, necessitate that (B)’s decision is coerced, or that (B)’s consent is insufficient. According to Wertheimer, it is necessary to make a distinction between moral faults in (B)’s background situation, and moral faults in the transactions that occur within that situation (ibid. p. 7, 69, 74-77, 206).
Furthermore, Wertheimer clarifies that the validity of (B)’s consent, could be undermined by faults in (B)’s information. Informational deficiencies might, for example, be due to fraud, or that (A) might withhold, or perhaps fail to reveal information that (A) has an obligation to provide. Consequently (B)’s consent to, let us say, surgery is not valid if (A) fails to inform (B) of the risks that are involved. However, even though (A) provides (B) with all significant information, (B) might not have the competence, due to e.g. mental disability or lack of adequate education, to process that information, to give valid consent to some interactions or transactions, or to make reasonable evaluations of the possible alternatives. An unfair transaction may however be exploitative even if (B)’s decision is well informed and rational, given the objective situation in which (B) has the competence to find himself/herself (Hawkins & Emanuel 2008, p. 7, 69, 74-77, 206).

3.2. Clinical Research

New therapies or procedures are regularly first tested by researchers in laboratory and in animal studies, whereas the most promising laboratory outcome are moved into clinical trials. Clinical trials are generally defined as biomedical or health-related research studies in human beings, which follow a predefined practice. The clinical trial process depends on the kind of trial being conducted. It could for example involve observational or interventional sort of research such as; “prevention trials” that look for better ways to prevent disease in people, using approaches such as medicines or vaccines. Clinical trials are conducted in stages; where each phase has a different purpose and help scientists answer different questions. Clinical trials are sponsored or financed by a variety of organizations or individuals such as medical institutions, foundations, and pharmaceutical companies, in addition to national agencies such as the National Institutes of Health (NIH), and the Department of Defense (DoD). Trials can occur in a variety of locations, such as hospitals, universities, or district clinics (Clinical Trials 2007). The clinical trial team consists of health care professionals such as doctors, nurses and social workers. Their responsibility is to examine the health of the participant at the beginning of the trial, provide detailed instructions for participating in the trial, monitor the participant carefully throughout the trial, and stay in touch after the trial is completed. Some clinical trials might e.g. require participants with illnesses, while others need healthy participants (Clinical Trials 2007).
Specific guidelines, such as the “ethical guidelines for biomedical research” that were initiated by CIOMS in 1993, are used by all clinical trials to enable decisions on who can participate. The use of “inclusion criteria” (the factors that allow someone to participate in a clinical trial) and “exclusion criteria” (the factors that disallow someone from participating in a clinical trial) is seen as a significant principle of medical research that helps to produce reliable results. These criteria are based on factors such as age, gender, the type and stage of a disease, previous treatment history, and other medical conditions. The criteria help to identify appropriate participants, keep the participants safe, and to ensure that researchers will be able to answer the questions they plan to study. People should know as much as possible about the clinical trial, before participating in it. They should feel comfortable asking the members of the health care team questions about it, regarding e.g. the care expected while in trial. In cases where participant's native language is not English, translation assistance should be provided. Participants should also be provided with an informed consent document by the research team containing details about the study, such as its purpose, duration, required procedures, key contacts, as well as an explanation regarding risks and possible benefits (CIOMS 2002; Clinical Trials 2007). Since the informed consent is not a contract, the trial participants are free to decide whether or not to sign the document, and may withdraw from the trial at any time. The ethical and legal codes that control medical practice are also relevant to clinical trials. In addition, most clinical trials are regulated with designed safeguards to protect the participants. To make sure that the risks are as low as possible and are worth any potential benefits, an Institutional Review Board (IRB) is recommended. An IRB is an autonomous committee of among other physicians, statisticians, and community advocates, whose obligation is to guarantee that a clinical trial is ethical, and that the rights of study participants are protected. As a clinical trial progresses, researchers report the results of the trial at scientific gatherings, to medical journals, and to a variety of government agencies. Individual participants' names should, however, remain confidential and not be mentioned in these reports (Clinical Trials 2007).
3.2.1. Risk of Exploitation

Concerns about exploitation in clinical research are evident, considering the fact that research “uses” the participants to gain generalizable knowledge. Consequently, all research participants are at risk of being exploited in clinical research, regardless if the research is conducted in high-income or low- or middle-income countries. Competent adults might for example, consent to being “used” in clinical research – yet, the form of “exploitation” in such cases does not necessarily have to be measured as morally worrisome. A more morally loaded sense of the term is, on the other hand, when exploitation involves “using” those who are “vulnerable”. However, considering that a large amount of ethically justified clinical research actually involves vulnerable research participants, e.g. people whom are seriously ill, the concept of “vulnerability”, similar to the notion of “use”, is merely a marker for moral concern and not a definite sign of moral violation. It is therefore considered to be possible to “use” those who are “vulnerable” without taking unfair or inappropriate advantage of their vulnerability (Hawkins & Emanuel 2008, p.12-14, 44).

3.2.2. Vulnerable Research Participants

CIOMS (Guideline 13) describes “Vulnerable individuals” as those who are moderately (or absolutely) incapable of protecting their own interests. They might e.g. have insufficient intelligence, education, resources, authority, or other required aspect to defend their own interests. Vulnerable individuals include e.g. children, women, institutionalized persons, impoverished people, and refugees, individuals who are politically powerless, whereas people who have serious or life-threatening diseases are described as highly vulnerable. It is not the gender or other group designation that are viewed as more open to harm, but rather their circumstances that create the vulnerability. For instance, women of child-bearing age (age 15-44) should be given the chance to take part in clinical trials, but they should on the other hand be well informed that research might incorporate risks to the fetus, if they become pregnant during research. Women are also, biologically, twice as likely as men to contract HIV in unprotected heterosexual intercourse from an infected partner. Consequently, women could be considered as biologically more complicated and, therefore, more vulnerable as research participants (OEC 2006; Reidar 2009; CIOMS 2002).
Furthermore, in accordance to the commentary on CIOMS Guideline 10: a vulnerable population could also refer to a so-called “underdeveloped community”. The term “underdeveloped” may, on the other hand, be questioned, taking into account that it does not take each country or community into consideration, regarding e.g. different levels of development. Communities might for instance be underdeveloped in an economical sense, and still be developed; by e.g. having a well functioning research review procedure and capacity to carry out certain research. So, even though low- and middle-income countries are categorized as generally more vulnerable to exploitation in comparison to high-income countries, it should not exclude the possibility that clinical research can be conducted in low- and middle-income countries, without taking unfair advantage of research participants (OEC 2006; Reidar 2009; CIOMS 2002; The World Bank 2010b).

Clinical studies that involve human participants entail careful consideration and case-by-case review. Considering that certain individuals and populations are more vulnerable as human research participants than others, require further protection in research. The main issue that have been raised in view of involving vulnerable populations in research, is that it might entail an unfair distribution of the burdens and benefits of research (OEC 2006; Reidar 2009). In medical research, a “risk” (or burden) generally refers to the possibility of any physical, psychological, social, or economic harm, as a consequence of taking part in a research study. The “benefit(s)” on the other hand, constitutes a desired outcome, either of new scientific knowledge or of improved health for the research subjects, or others (OHRP 2010).

3.2.3. The Risks/Burdens from a Transaction

In studies intended to evaluate treatment for life-threatening illness, risk of side effects might actually be acceptable. In research where no direct benefits to the subject are expected, an Institutional Review Board must evaluate whether the probable risks are ethically acceptable, while considering the importance of the knowledge that possibly will result from the research. If the study only involves so-called “minimal risks” IRBs are not required to protect competent adult subjects from participating in non-beneficial research procedures. However, there are different opinions and no specific standard on what might constitute a sufficiently low risk, or minimal risk, in this context (Wendler 2009; OHRP 2010).
A typical view that can be found in several guidelines, such as the U.S. Department of Health and Human Services 2005, is that non-beneficial research is ethically acceptable as long as the risks do not exceed the risks subjects face in daily life. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination. What might be considered as problematic with the “risks of daily life” standard is that it does not prevent the probability of some subjects experiencing serious harm. For instance, there is a chance of serious harm from many of the activities of daily life, such as crossing the street. Yet, such “low risks” of daily life are often ignored by psychologically healthy individuals, unless the circumstances provide reason for special concern (e.g. the sound of a siren). However, let us assume that an adequate amount of “minimal risk” research are carried out during a certain period of time - might there not be a probability that a few subjects eventually will experience some kind of serious and enduring harm? Another issue is that a risk, that might be measured as “minimal” to one person, could in fact be dangerous to another. For instance, an outdoor exercise might be dangerous to people with asthma, if the air is polluted or saturated with allergens; or taking a blood sample, might be a great risk to a hemophiliac; who is diagnosed with a rare bleeding disorder in which the blood doesn't coagulate normally (Wendler 2009; OHRP 2010).

Keep in mind that, decision about estimated risks and benefits of interventions in research, often depend on currently available information that is drawn from animal research. Such type of information is on the other hand beyond question, since human responses to a certain scientific intervention could differ from those of animals. And just because data regarding risks might be missing, does not necessarily indicate that no risks exist (OHRP 2010). Furthermore, as what already have been mentioned, is that a risk is not only related to the physical health of a person. Taking part in clinical trials could also cause social harm, having a negative effect on the trial participant present or future life situation. Areas of particular sensitivity include research regarding among other, alcohol or drug abuse, mental health, and sexual behavior. Consequently, participating in e.g. HIV-related drug trials could “label” or stigmatize the subjects, limiting their opportunity regarding among other, employment, or position in the community in general (Wendler 2009; OHRP 2010).
3.2.4. The Benefits of Research

Access to HIV treatment has been an issue for a long time, particularly in low- and middle-income countries. A significant explanation has to do with the matter of high prices of antiretroviral drugs (ARVs) and international patents. But in 2001, special terms in the international trade law, made it possible for drug manufacturers in low- and middle-income countries to start producing generic drugs (“Me-too” drugs) at cheaper prices. As a result, HIV treatment was possible to expand on a global scale. However, the number of people in need of treatment continues to increase, and access to ARVs is still insufficient for many people living in low- and middle-income countries. Yet, having access to HIV treatment does not necessitate that the drug is of good quality or the most effective treatment available on the market. For instance, “Me-too” products are structurally very similar to drugs already in use, and can therefore only provide minimal health benefits. “Me-too” products do, on the other hand, have the potential to generate competition and deliver lower prices, which medical companies could gain large profits from. Bearing in mind that pharmaceutical companies, just like many other industries, seek the best value for money and maximization of profit, could lead companies to track new medical treatments which might not even have any potential to improve health and well being (Medicine Net 2010; AVERT 2010; Wendler 2009).

Financial motives have been identified as one of the leading factors behind pharmaceutical companies increased interest of having research projects carried out in low- and middle-income countries. Pharmaceutical companies might for example lower their costs by relocating medical trials to low- and middle-income countries instead of having research conducted in high-income countries, such as the United States and countries in the European Union (EU). Cases involving collaborative research, between research-groups in high-income countries and low- and middle-income countries are often of special concern. The concern is somewhat related the probability that socioeconomically disadvantaged groups might be recruited as research participants in low- and middle-income countries to test drugs designed for sale in high-income countries. The moral worry is, however, usually about the huge profits that multinational drug companies collect from knowledge gained by medical research (Glickman, McHutchison, et al. 2009; Wendler 2009).
For instance, according to the IMS Market Prognosis (an industry indicator of market dynamics and therapy performance), the value of the global pharmaceutical market is expected to make USD880 billion, in 2011, whereas the United States will remain the single largest pharmaceutical market. Pharmaceutical sales in the United States are expected to generate more than USD320 billion (with a 3-5 percent growth) in 2011 up from USD310 billion forecast for 2010 (IMS Health 2010). Consider these statistics; the hundreds of billions of dollars that pharmaceutical companies are estimated to gain from the development of a medical treatment, one might question what would constitute a fair response to the participants, whose involvement is of great importance to the development of the medicine in question. However, distinguishing what might be a fair level of benefit to the research participants is more of a complex task, where several ethical aspects have to be taken into consideration. Offering volunteers paid compensation for their participation in research, is such an example (Wendler 2009). Some have argued that financial compensation in research should be avoided, with the exception of some limited circumstances. According to for example the United States Department of Health and Human Services, financial encouragements are mainly used in certain trials when health benefits to participants are remote or nonexistent. Research volunteers are in such cases compensated for the amount of time that has been dedicated to the trial, along with the level of discomfort that might occur during the study. Information regarding paid compensation should be discussed with potential research participants during the informed consent process, and should be documented in the informed agreement. Yet, financial compensation in research remains controversial. There are for example no joint agreements regarding correct amount of payments. And even if it has been claimed that this type of practice should be restricted, compensation for participating in research have been portrayed as quite common (FDA 2009; Slomka, McCurdy, Timpson, et al. 2007).

A typical ethical concern is that impoverished populations, as well as other vulnerable populations, might be easily recruited to take part in research for a small amount of money, and that paid compensation might encourage participants into more risky behavior. In a scientific report, published in 2007, research participants among adult African-American drugs users in Houston, Texas, were interviewed regarding their financial motivations for participating in HIV research. The participants rejected the idea that financial compensation encouraged drug use, or risk taking. In general, the participants considered payment for research as necessary enable to attract interest. Paid compensation was also seen as an additional income source (Slomka, McCurdy, Timpson, et al. 2007).
Most respondents considered USD20 as an appropriate amount of payment for participation in HIV behavioral research. Lower payments as USD5 or USD10 were viewed as ineffective as a recruitment encouragement, as well as unfair to research participants. The study clearly demonstrates that financial compensation is a crucial part when potential participants decide to take part in research projects. But, even though participants in this particular study rejected the idea that payment in research might encourage participants into more risky behaviors’ does not exclude the probability that it actually could be the case in another context (Slomka, McCurdy, Timpson, et al. 2007). Besides financial compensation, it should also be acknowledged that health benefits are a significant motive for participating in research. The ESPIRIT study was carried out in 2008, with a focus on individuals’ motivations for continued participation in HIV clinical research. It involved 117 participants, including HIV-infected men and women, from Argentina, Brazil and Thailand. In sum, the findings revealed that more than 80 percent of the respondents considered the opportunity to attain medical or personal benefit, as very important motives for continuing to partake in the study (Wendler, Krohmal, Emanuel, et al. 2008).
4. RISK ASSESSMENT

It has already been clarified that the status of the parties is irrelevant in determining whether exploitation has occurred. If the exchange is fair to both parties, then there is no exploitation regardless of whether one party is vulnerable or not (Hawkins & Emanuel 2008, p.294). But on the other hand, the intention of this particular study is to evaluate the risk of “high-risk women” being exploited as research participants in HIV clinical research, and not to determine whether high-risk women have been exploited. In addition, that one party is vulnerable might in fact make exploitation more likely to occur. For that reason, I find it necessary to examine the status (vulnerability) of the target group. Furthermore, enable to evaluate the risk of exploitation; I consider it important to look at the probable outcomes (risks and benefits) from a potential transaction, between researchers and high-risk women. I will also examine the efficiency and reliability of the so-called “control mechanism” for research, which refers to ethical guidelines and regulations, and Institutional Review Boards. Ethical codes for clinical research and Institutional Review Boards are essential safeguards to minimize the possibility of exploitation, by for example ensuring that research subjects are treated with respect, and provided with an informed consent document regarding risks and possible benefits, among other (Hawkins & Emanuel 2008, p.13; Clinical Trials 2007).

Table 1: Risk Indicators

<table>
<thead>
<tr>
<th>Risk Indicator</th>
<th>Increased Risk</th>
<th>Decreased Risk</th>
</tr>
</thead>
</table>
| 1. “Vulnerability as research participants” | High-risk women are measured as vulnerable as research participants
                             ........................................................................
                             High-risk women’s circumstances create a vulnerability that are more open to harm, and exploitation | High-risk women are not measured as vulnerable as research participants
                             ........................................................................
                             High-risk women’s circumstances does not create a vulnerability that could be exploited |
| 2. “Possible risks/burdens”     | The possible “risks” (such as physical, social and economical harm) as a consequence of enrolling high-risk women in HIV clinical research are measured as high | The possible “risks” (such as physical, social and economical harm) as a consequence of enrolling high-risk women in HIV clinical research are measured as low |
### Risk Indicator

<table>
<thead>
<tr>
<th>Risk Indicator</th>
<th>Increased Risk</th>
<th>Decreased Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. “Possible (unfair) benefits”</td>
<td>The possible benefits from a transaction are measured as unfair</td>
<td>The possible benefits from a transaction are measured as fair</td>
</tr>
</tbody>
</table>
| 4. “Efficiency & reliability of the control mechanism” | • The “control mechanism” for research is measured as inadequate to handle a trial in the specific Cambodian context.  
• There is a risk that the Cambodian ethical review board is affected by inappropriate influences. | • The “control mechanism” for research is measured as efficient to handle a trial in the specific Cambodian context.  
• The Cambodian ethical review board is considered to be free by inappropriate influences. |

### 4.1. Risk Assessment Tool

A risk assessment tool will be applied in the following chapter, enabling to estimate the level of risk of Cambodian high-risk women being exploited as research participants in HIV clinical research. The risk assessment tool consists of four risk indicators: (1) vulnerability as research participants, as regards to high-risk women’s vulnerability as potential research participants in HIV clinical trials; (2) the possible risks and burdens from a transaction, when involving high-risk women in HIV trials; (3) possible unfair benefits from a transaction; and (4) the efficiency and reliability of the control mechanism for clinical research. In view of the contextual circumstances of Cambodian high-risk women, and the context of Cambodia, each indicator will separately signify whether there is an increased or decreased risk of Cambodian high-risk women being exploited as research participants in HIV clinical research (Tab. 1).
### Table 2: Risk Assessment Tool

<table>
<thead>
<tr>
<th>Risk Indicator</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Risk of Exploitation</th>
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<tbody>
<tr>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>Moderate</td>
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<td></td>
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<td>Moderate</td>
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<tr>
<td></td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Low</td>
</tr>
</tbody>
</table>

(+): Increased risk of exploitation  
(-): Decreased risk of exploitation

In conclusion, if four (out of four) risk indicators reveal that there is a decreased risk of exploitation; it will be estimated that there is a low risk of exploitation. However, if one or two, out of four, risk indicators signify that there is a decreased risk of exploitation, then it will be concluded that there is a moderate level of risk of exploitation. And finally, if three or four, out of four, risk indicators reveal that there is an increased risk of exploitation, it will be estimated that there is a high (great) risk of Cambodian high-risk women being exploited as research participants in HIV clinical research (Tab.2).
5. CONTEXT ANALYSIS: CASE CAMBODIA

In collaboration with institutions in the development and conduct of HIV/AIDS and sexually transmitted diseases related research, NCHADS have formed a research unit, supported by a research steering committee, with the aim to improve the prevention and care interventions as well as to create an HIV/AIDS-related research agenda. The agenda is intended as an instrument for both national and international researchers on the significance of research proposal. To ensure that the cooperation is carried out in the best interests of people living with HIV and AIDS (PLHA) in Cambodia, the joint research program is supervised by among other; a steering committee including the director of NCHADS research unit, and a representative of funding organizations. The steering committee is counseled by an independent review board, including key members of institutions involved with HIV/AIDS in Cambodia, and a PLHA forum including a representative board of PLHA in Cambodia. All public and private institutions involved in HIV examination have to be qualified and supervised by the Ministry of Health; strictly follow the ministry guidelines; be run by personnel skilled under approved courses; and report regularly to NCHADS using standardized formats (NCHAD 2007; NCHADS 2009). The guidelines for testing in Cambodia and provisions for confidentiality are stated in the Cambodian Law on the Prevention and Control of HIV and AIDS, 2002 (Chapter IV & VII). All trials should be voluntary with the informed consent of the individual. Research that involves anonymous testing have to be granted by the Ministry of Health (MoH), and its ethics committee, and confirmed by the ministry’s ethical guidelines for HIV and AIDS related research (NAA 2008).

According to the WHO Country Cooperation Strategy (2009-2015), around 20 multilateral and bilateral donors and more than 100 health-related international and national NGOs participate in the Cambodian health sector. Research in prevention is referred as a key component in Cambodia’s strategic HIV/AIDS plan and has steadily increased since 1995. A total number of 143 out of the 255 studies that have been conducted in Cambodia since the early eighties, accounts for prevention research. Out of these, 58 percent have been carried out as socio-behavioural research; 26 percent with an epidemiological research design; 9 percent focus on response analysis; whereas 6 percent have a clinical research design (NCHAD 2007; NCHADS 2009; WHO 2009b).
However, it was not really before the planning of the so-called “tenofovir trial” in which Cambodia became practically familiar with involving highly vulnerable populations in prevention trials. The groundwork and background research of the trial began in the late 2002. It was approved funding in 2003 and later the same year, a preliminary trial protocol was presented to the Cambodian Ethical Review Board that was subsequently approved, allowing the research team to start preparing for the trial. The trial which included commercial sex workers were, however, halted by the Cambodian government, in 2004, because of lack of agreement on future access to medical and health care treatment for those who became infected during the clinical trial (UNAIDS 2007; Global Campaign for Microbicides 2009).

According to the IFPMA Clinical Trials Portal, there is only one clinical trial that is currently active in Cambodia with relevance to HIV-research, involving adult female participants. The research participants do not on the other hand include high-risk group women. Instead, the ongoing trial (NCT00334256) enrolls pregnant HIV-infected participants of 28-38 weeks of gestation. The trial is sponsored by the French National Agency for Research on AIDS and Viral Hepatitis, in collaboration with the European and Developing Countries Clinical Trials Partnership (EDCTP) and Gilead Sciences. The aim of the study is to evaluate the safety and the resistant patterns of a combination drug (tenofovir and emtricitabin). Further information regarding the trial is available on the IFPMA Clinical Trials Portal (IFPMA 2010).

Even if high-risk group women are not being recruited as research participants in HIV prevention trials at the moment, in accordance to the IFPMA Clinical Trials Portal, does not exclude the probability that they might be in the near future. According to the Parliamentary Handbook on HIV and AIDS, the HIV prevalence rate in the adult Cambodian population aged 15 to 49 has fallen from 2 percent in 1998 to an estimated 0.7 percent in 2009. But, even if the recent years have shown that it has been some improvement in the health outcomes, the health status is still worrying, being among the lowest in Asia. In accordance to the United Nations Development Programme (UNDP), the main challenges at the moment are to retain and improve HIV prevention, as well as to reduce the risk transmission among the Cambodian high-risk population. Considering that female sex workers and injecting drug users are estimated as two out of three central most at risk populations in Cambodia, there are good reasons to believe that the HIV research community will find them interesting as appropriate clinical participants (Cambodian Parliament 2010; UNDP 2010ab).
In contrast to HIV treatment trials, which involves individuals that are already HIV infected, prevention trials enroll “healthy” (non-HIV-infected) individuals enable to observe whether the intervention reduces their risk of acquiring HIV infection over time. Since HIV transmission is quite infrequent, prevention trials need to engage a large number of high-risk individuals. A typical HIV-prevention strategy is when HIV-negative people take an ARV drug on a regular basis prior to HIV exposure, with the aim of preventing HIV infection. This type of strategy is also known as PrEP trials; as pills (oral PrEP), or gels (topical microbicides) are used as pre-exposure prophylaxis (AIDSTAR-One 2009; FHI 2010). Tenofovir was for example tested as an oral PrEP in clinical trials launched in 2004, including the Cambodian tenofovir trial. Tenofovir disoproxil fumarate is an oral antiretroviral drug which is marketed under the trade name “Viread” by Gilead Sciences, a US-based biopharmaceutical company. It should be pointed out that Gilead Sciences was not involved in the planning, implementation or funding of the Cambodian tenofovir trial. Gilead did however provide the trial with medication and placebos (Global Campaign for Microbicides 2009). The ARV drugs “Viread” and “Truvada” (a combination between emtricitabine and tenofovir disoproxil fumarate) are currently being tested in PrEP trials conducted in several countries located in among other Asia, South America, and Africa (FHI 2010).

5.1. Risk/Benefit Evaluation

The Human Development Bank classifies Cambodia as a low-income country (according to 2009 GNI per capita, “low income” is referred to as USD995 or less). Cambodia’s Human Development Index (HDI) is ranked as 124 being below the regional average. HDI represents a broader definition of the well-being and human development of a nation, including health, education, and income (Human Development Report 2010; The World Bank 2010ab).

In addition, Cambodia is categorized as an extremely resource-poor country. The public medical system in Cambodia is so poor that at least one-fifth of the Cambodian population lack access to medical health care services. The Cambodian health system is funded by international aid programs and international nongovernmental organizations and by charging user fees to patients. Health care services could for example cost a single household as much as one third of a family income, whereas illegal charges in public facilities are not an unusual occurrence (Human Rights Watch 2010; WHO 2001; Utrikespolitiska Institutet 2009).
Consequently, health care expenditures have become a significant cause of indebtedness among the impoverished population of Cambodia. Travel distance and high costs of transportation, are further reasons why poor access to health care services is a particular issue amongst the impoverished population living in the remote rural areas of Cambodia. But in several cases, lack of accessible health treatment, is rather a matter of discrimination and not necessarily about affordability, or availability of health services. People living with HIV and people with risk behaviors’ for HIV, including female sex workers, is among the most marginalized population in Cambodia. They are avoided by their families, thrown out from homes and communities, and often denied health care (Human Rights Watch 2010; WHO 2001; Utrikespolitiska Institutet 2009). There are no exact numbers of sex workers in Cambodia. Such estimation would on the other hand be difficult to achieve since many forms of sex work are illegal. The different forms of prostitution are generally based on the locality, age, or situation of the commercial sex worker. Some might for example carry out their work in their own homes, under the management of a brothel-owner, as a singer in a karaoke bar, as a “beer girl”, a masseur, or perhaps as a homeless person on the street. Adult female sex workers, are generally considered as "used goods" (in comparison to virgins) and have therefore a lower value and might gain as little as USD2 per customer. Female sex workers suffer miserable conditions and abuse, including domestic violence, sexual abuse, rape, and little or no protection against sexually transmitted diseases (Human Rights Watch 2010; Hughes, Sporcic, Mendelsohn, et al. 2010). In view of these circumstances, it is likely to believe that a number of high-risk women might eventually agree to participate in research enable to receive possible benefits that they otherwise might not have been able to obtain. Such offers might for example include free medical- or health care treatment, or a certain amount of money. Some of these women might even participate in research since they would feel protected by the benefits they possibly been offered. But before taking part in prevention research, potential participants are expected to reflect on whether the benefits which they might gain from a certain transaction are fair in comparison to the possible risks. There are for example no reliable data on possible side effects on ARV drugs, such as the tenofovir, on non-HIV-infected individuals, testing the drug might therefore lead to further harm which has not yet been recognized. Scientific findings, based on the experience of individuals with HIV infection, have for example shown that tenofovir disoproxil fumarate might cause serious side effects including liver problems or a condition called lactic acidosis, which in some cases could have deadly outcomes (EMEA 2005; Gilead 2010; FHI 2010; Global Campaign for Microbicides 2009).
Tenofovir might also cause kidney damages or decreases in bone mineral density which eventually could lead to osteoporosis, whereas diarrhea, nausea, and headache, are among the most common side effects that have been documented (EMEA 2005; Gilead 2010; FHI 2010). Taking into account that some of the side effects such as damage to internal organs might not be visible for many years, it is found important that research participants are followed-up during a longer period of time. As regards to the Cambodian high-risk women’s circumstances, the likelihood of affording or having access to health controls on a regular basis could be predicted as quite small. It might therefore be suggested that high-risk women whom participate in prevention trials, should be offered free treatment for side effects during the course of the trial as well as after it has been completed. Additionally, the participants might be more likely to attend follow-ups if the study centre is located somewhere nearby their residences, considering possible travel distance, and access to an affordable transportation option, which otherwise might have been a hinder. Enrolling high-risk group women in prevention trials in Cambodia might, on the other hand, entail more harm to the research participants besides the possible side effects from an antiretroviral drug. Common side effects such as diarrhea could for example have a negative impact on the research participants’ livelihood; hindering the female sex worker from being able to accomplish her job, which might not only affect the commercial sex worker herself but also other people whom may be dependent on her earnings. Further concern is that high-risk women, whom participate in prevention trials, may engage in more unsafe behaviors which could increase the risk of HIV infection. Research participants may for instance judge condom use as unnecessary, or use dirty or shared needles, having the false belief that the ARV drug would protect them from receiving HIV infection. Unsafe practices can also be a matter of not being able to afford, or having access to “safety measures” such as condoms, clean needles and syringes. Providing female sex workers with condoms and clean needles might therefore reduce the spread of HIV infection. It is also necessary that the potential research participants are accurately informed about the trial and the possible risks, and that they recognize the details presented in the informed consent. However, considering the serious health conditions that illicit drugs, such as methamphetamine, could cause injecting drug users, such as brain damage, memory loss, and psychotic-like behavior, increases their vulnerability as research participants. Enrolling injecting drug users in prevention trials could therefore involve the risk that some of the potential participants might not be capable of recognizing the goals of the study, or providing informed consent, due to possible mental disability (O’Connor 2008; NIDA 2004).
Some of the potential participants might, on the other hand, continue to practice unsafe sex during the course of the trial, even if they are provided with free condoms, and are fully aware of the possible risks and the importance of using protection. Three possible explanations for such behavior may be related to: (1) drug addiction; (2) fear to resist the pressure from male clients desire to engage in unprotected sex; and (3) poverty, as regards to financial insecurity and an urgent need for an additional financial compensation (Human Rights Watch 2010). However, HIV prevention trials are in fact based on the reality that some of the research participants will be incapable or unwilling to use “prevention packages” such as free condoms or risk reduction counseling. Consequently, some of the participants might become HIV infected during the course of the trial, making it possible for HIV-prevention trials to assess the impact of the test intervention (Global Campaign for Microbicides 2009). And those who eventually do become HIV-infected might not even have access to available treatment. As previously mentioned, high-risk women as well as people with HIV-infection are among the most discriminated population in Cambodia, who are frequently, denied health care (Human Rights Watch 2010).

In view of the context of high-risk women, it is found to be less likely that “healthy volunteers” would agree to accept the side effects of an antiretroviral drug, or other related risks, while taking part in a trial, in which the profit is based on using it as a treatment for people whom are HIV-positive. Whereas, people whom are already HIV-positive when taking part in a treatment trial might be more willing to accept side effects of a drug in hope that the treatment being tested will help to lengthen or save their lives. However, if the drug tested in a prevention trial, proves to be able of preventing HIV infection, then it might actually benefit any person whom the drug prevents from being infected, including high-risk women. On the other hand, if such drug would be available on the market, it would not necessarily indicate that Cambodian high-risk women would have access to, or manage to pay for such drug.

Many governments in the Asia-Pacific region, including Cambodia, spends little public money on health care, which have resulted in very high levels of private health expenditure, a large amount of it “out-of-pocket”. In this case, an out-of-pocket cost represents the cash expenses that a patient has to pay directly to the health care provider, money which may not be repaid later on (Cheng 2010). Consequently, even if an effective (PrEP) drug would be offered for free, many high-risk women would probably have to pay considerable out-of-pocket costs which they would be very unlikely to afford.
So, what about financial compensation? The possibility of receiving an additional amount of payment for participating in a clinical trial might be considerably appealing for high-risk women, with particular regard to their economical situation. But what is rather unclear in this matter, is what would have to constitute a fair compensation, when involving a vulnerable population, such as the Cambodian high-risk women, in prevention trials. In view of the draft protocol for the Cambodian “tenofovir trial”, for instance, research participants were promised USD3 per month as compensation for taking part in the trial for 12 months (Global Campaign for Microbicides 2009). Taking into account that the mean monthly income of rural female sex workers in Cambodia were documented as USD60 in 2003, one might consider the USD3 compensation as rather unfair, with particular notice to the risks prevention trials might entail (Sopheab, Gorbach, Gloyd, et al. 2003). The small amount of payment that the research participants might be compensated could also be measured as unfair in comparison to the billions of dollars that pharmaceutical companies may benefit from the knowledge gained from the same transaction (IMS Health 2010).

5.2. Estimated Risk of Exploitation

In view of the context of high-risk women, it is considered quite unlikely that high-risk women whom might participate in prevention trials, conducted in Cambodia, stands to benefit from the results of that research. Non-beneficial research might, on the other hand, be ethically acceptable in some cases, as long as the risks are low, and do not exceed the risks subjects face in daily life. However, as previously mentioned (in chapter 3.2.3) the “risks of daily life” standard does not consider the probability of some subjects experiencing serious harm. For instance, the risks female sex workers (and female sex workers whom inject drugs) face in daily life, is rather high than low. The risk of daily life standard is for that reason not considered as an appropriate tool when enrolling high-risk women in prevention research. The risk of daily life standard might in fact be used as an excuse, to expose high-risk women to serious harm. The risk of becoming HIV infected during the course of a trial could perhaps be excused as being up to standard, considering the risk (of receiving HIV infection) that the participants already face in daily life, as commercial sex workers. However, even though the so-called “daily risks” would refer to those earlier examples presented in chapter three, such as crossing the street, or an outdoor exercise, it would still engage certain risks. Yet, the
estimated “level of risk” (high/low risk) would almost certainly differ in various cases. It has for example already been clarified that prevention trials might entail risks that in some cases might include damages to internal organs, or HIV infection. Even minor side effects might hinder participants’ ability to work which could result in hunger and insecurity. In view of the rather unsafe as “minimal” risks prevention trials might entail potential research participants, along with the likelihood of not receiving a fair benefit from the result of the research, increases the risk of exploitation.

Enrolling high-risk women in prevention trials, in Cambodia, necessitate careful consideration, and case-by-case review, as regards to their vulnerability as research participants. It is therefore of great significance that NCHADS have developed a control mechanism for research, including ethical guidelines and regulations as well as an independent review board, in effort to avoid unethical trials, and to protect human participants from exploitation. The efficiency and the reliability of the control mechanism could on the other hand be questioned. One of the concerns regard the fact that corruption has been documented to be widespread throughout the country. According to the Transparency International Global Corruption Barometer 2009, the civil service is perceived as the most corrupt sector in the Asia Pacific region, including Cambodia, where about 1 in 10 indicated that they had paid a bribe (Transparency International 2009). Considering the power that corruption entails, permitting political and financial interests to control different sectors of the society – one might question, whether the Cambodian review board is free from inappropriate influences. An independent review board is a fundamental instrument enables to protect potential research participants from exploitation, taking into account that pharmaceutical companies are highly dependent on institutional review boards’ conclusions (whether possible research projects are found ethically acceptable to be carried out, or not). However (as previously mentioned in chapter 3.1.1), even though a transaction might be judged as unethical, does not have to be an indication that it is a matter of exploitation. For instance, a corrupted review board might agree to unethical research projects – but, it does not necessary mean that the researchers are exploiting the participants. On the other hand, a corrupted IRB might withhold information, regarding for example, the risks that are involved in a clinical trial, which consequent ly would influence the validity of the research participants consent. It is therefore possible to assume that a corrupted review board might promote an unfair transaction, which may be exploitative.
Cambodian research reviews could, however, be free from corruption and inappropriate influences, and still be accused as morally wrong; approving research which some might regard as unethical, or even exploitative. For instance, it has already been clarified that principles, such as the “risk of daily life” standard, may be open to interpretation and does not necessarily recognize contextual dissimilarities in various cases. Consequently, review procedures may be applied in accordance to particular standards which may not, on the other hand, be applicable on different contexts. Collaborative research, between research-groups in high-income countries and low- and middle-income countries are of particular concern. Enrolling high-risk women in HIV-prevention trials in the United States, for instance, would probably involve dissimilar circumstances in comparison to the Cambodian context. It is therefore found to be of great importance that contextual dissimilarities are recognized as review procedures are applied, regarding e.g. the legal mechanism, or the health system of the host country, or perhaps the level of education amongst the potential research participants (Reidar 2009; Landes 2005). In the preparation of the Cambodian tenofovir trial for instance, NCHADS had worked with the University of California; San Francisco to guarantee the Cambodian Ethics Committee’s an education that was compatible to the National Institutes of Health (NIH) standards. The NIH policy was adopted in 2000, and lays out specific training requirements that apply to all NIH grant recipients. But, even though the protocol for the Cambodian tenofovir trial had passed review procedures compatible to the NIH standards, the Cambodian authorities accused the trial for being unethical and incompatible with the international standards of research ethics. A question that has been raised is whether the NIH standards that were applied in the review process of the tenofovir trial were adequate enable to handle a trial in the specific Cambodian context, at that point in time (Global Campaign for Microbicides 2009). A similar question could be asked with relevance to the Cambodian existing context. Enable to approach the needs and priorities of potential research participants, necessitate that their contextual circumstances are taken into consideration. Considering the high level of funding that the Cambodian health sector receives from e.g. international aid programs and organizations, along with the collaborations that are made in HIV research, raises concern. The concern involves the risk that the Cambodian ethical review board might approve cases, in accordance to certain standards that might be appropriate to the context of the funding and collaborative countries but not necessarily to the Cambodian context, and the context of high-risk women.
Furthermore, determination of whether the distribution of benefits from a transaction is fair depends on the level of benefits received by the population of the community enrolled in the research. It is the research participants who bear the burdens of the interaction, and are at risk of exploitation. However, there is currently no joint agreement of an international standard to fairness or a so-called “normative standard” which Wertheimer recommends, enable to evaluate the fairness of the level of benefits from a transaction (Hawkins & Emanuel 2008, p.299, 73). It is, for example, not possible to determine the value of the benefit to the research participants merely by comparing the transaction to a similar case. What might represent a fair level of benefit to high-risk women in Phnom Penh, Cambodia, are likely to differ, in comparison to what high-risk women in, for example, Houston, Texas, United States, might consider as fair. It is, therefore, once again important to recognize the contextual dissimilarities between cases.

- So, if the “control mechanism” is insufficient or unreliable, and therefore not capable of protecting the interest of high-risk group women as potential research participants, then who possibly will?

Organizations for sex workers are mainly run with support from other NGOs and have a significant task in representing the interests of sex workers, advocating on behalf of sex workers and their members with e.g. the government, organizations, and multilateral institutions. The leading organization for sex workers in Cambodia is Women’s Network for Unity (WNU). The network operates as a nongovernmental organization, and has about 5000 active members in 13 provinces and cities in Cambodia. Since the network was formed, in 2000, sex workers have gained the courage to speak out about their problems. One of the most controversial protests involved the tenofovir trial. WNU questioned the trial in terms of its ethics and process, and required, among other, that the researchers running the trial should offer the participants health insurance for 20-30 years for the possible long term side effects of tenofovir (WNU 2010; Global Campaign for Microbicides 2009; AIDS_Asia Forum 2005). One could say that the tenofovir trial expanded the view of research, and conduct of clinical trials, particularly among the women in the sex worker community. Raised awareness of possible risks, benefits and research procedures, empowers high-risk women to stand against unfair and perhaps exploitative research proposals. Yet, it does not reduce the possibility of high-risk women being convinced to participate in research in exchange of e.g. paid compensation or other offers, that they have a need for, or have a difficulty to access.
Such offers might not, on the other hand, have been so appealing for high-risk women under different circumstances; if they for example earned their living in a safe environment, free from threats and social stigma; if they were free from drug addiction; or if they had access to affordable health care services (WNU 2010). It is therefore highly important that the rights of female sex workers are supported by, among other, organizations such as the WNU, to minimize the risk of pharmaceutical companies taking advantage of high-risk women’s unfair conditions. However, since the implementation of the “prostitution pledge” and the new law on Suppression of Human Trafficking and Sexual Exploitation, the vulnerability of female sex workers have increased and several organizations have not been capable of continuing their work. In May 2003, the U.S. congress passed the United States Leadership against HIV/AIDS Tuberculosis and Malaria Act. The act which is also known as the so-called “prostitution pledge” prohibited the use of federal funds to promote, support or advocate the legalization or practice of prostitution. Foreign organizations, including several donors and NGOs that once worked with Cambodian sex workers, consequently had to accept the pledge in order to receive U.S. funding. HIV prevention initiatives, including e.g. the distribution of condoms, women empowerment programs and drop-in centers, where consequently withheld from sex workers (Alfirev 2009). And in 2008, a new Law on Suppression of Human Trafficking and Sexual Exploitation was introduced in Cambodia. The law does not criminalize clients of adult sex workers. Adult sex workers are not, on the other hand, legally allowed to solicit in public, whereas procurement for prostitution, as in providing a person for sexual services, is defined as a criminal act, in accordance to the 2008 “Law on Suppression”. However, under article 25 (3) “procurement” is also described as any act that might be “...hindering the act of prevention, assistance or reeducation undertaken either by a public agency or by a competent private organization for the benefit of persons engaging in prostitution or being in danger of prostitution” (The law on Suppression of Human Trafficking and Sexual Exploitation). Consequently, anyone who has any identifiable connection with sex work, including e.g. sex worker organizations, might be charged with procuring (Human Rights Watch 2010). The law have been criticized for have had an adverse effect on outreach and access of public health services to commercial sex workers. The law has also contributed to an increased social marginalization and stigmatization of sex workers, and has led to numerous human rights abuses. As a result high-risk women’s vulnerability as research participants has become greater than before. Participation in research would almost certainly reveal high-risk women’s association to the sex sector. The fear of being caught might therefore minimize their interest of taking part in a trial. However, in desperate circumstances, free access to health care
services might for instance be prioritized over the possible risk of being caught. In addition, the law on Suppression of Human Trafficking and Sexual Exploitation does not seem to have had a negative impact on pharmaceutical companies’ possibility of enrolling high-risk women in research, in Cambodia. For instance, an HIV trial (NCT00226434) which involved adult female sex workers, were completed, in 2010 (IFPMA 2010). However, considering that the start date for the trial occurred in 2006, entails that the research participants probably had been recruited before the law was put into practice. Yet, the trial was not halted for enrolling female sex workers and was able to continue its process, despite the law.

- Are Cambodian “high-risk women” at great risk of being exploited as research participants in HIV trials?

<table>
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<tr>
<th>Risk Indicator</th>
<th>Increased Risk</th>
<th>Decreased Risk</th>
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<tr>
<td>1. Vulnerability as research participants</td>
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<tr>
<td>2. Possible risks/burdens</td>
<td>X</td>
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<td>3. Possible (unfair) benefits</td>
<td>X</td>
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<td>4. Efficiency &amp; reliability of the control mechanism</td>
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Risk of Exploitation: **High**

Enrolling Cambodian high-risk women in prevention trials might not only endanger their physical health, but also their economical and social situation. Injecting drug users might not be capable of recognizing the goals of the study due to possible mental disability, which could lead them into more unsafe behaviors, increasing the risk of receiving HIV infection. Additionally, not being competent to give valid consent increases the risk of a possible unfair transaction, and the probability of exploitation in research. Furthermore, high-risk women may not even be capable of earning an income during the course of the trial, because of minor side effects of the drug being tested. However, despite the possible burdens, high-risk Cambodian women are found very unlikely to benefit from the result of prevention research. They might, on the other hand, be compensated with a certain amount of money or promised
access to health care services, for participating in research. Such offers would most likely be appreciated by impoverished individuals whom are frequently denied health care due to stigma and discrimination. But even though prevention trials might be mutually beneficial, to a certain degree – the distribution of possible risks and level of benefits from a prevention trial are more likely to be unfair, increasing the risk of exploitation. To avoid having high-risk women’s unfortunate circumstances taken advantage of for the commercial interests of pharmaceutical companies requires that the Cambodian ethical review board is free from inappropriate influences. It is also required that the principles that are applied in the review process are adequate enable to handle a trial in the specific Cambodian context. But, due to e.g. corruption, high level of funding and collaboration in research, the efficiency and the reliability of the “control mechanism” for research might be jeopardized, increasing the risk that high-risk women’s contextual circumstances, and their vulnerability as research participants’ might be ignored in the review process of a trial. Consequently, Cambodian high-risk women are found to be at great risk of being exploited as research participants in HIV clinical trials (Tab.3).
6. CONCLUSION

In view of the social and economical situation of Cambodian high-risk women, it is found very unlikely that they would be able to benefit from possible research outcomes. Illegal charges in public facilities, large out-of-pocket expenses, and social and cultural discrimination, are some of the main issues that hinder high-risk women from accessing high quality health care services. In addition, laws governing prostitution, such as the “prostitution pledge” and the 2008 law on Suppression of Human Trafficking and Sexual Exploitation have increased the risk of violence and discrimination against Cambodian high-risk women. The set of laws have limited high-risk women’s access to health care services and increased their vulnerability as research participants. The so-called control mechanism for research are questioned whether it e.g. is capable of handling research evaluations in a correct and reliable way, enable to protect Cambodian high-risk women from exploitation in research. Consequently, a weak control mechanism for research may allow HIV clinical trials to take unfair advantage of the reality that numerous of Cambodian high-risk women lack access to high-quality and affordable care, and therefore may accept offers that could provide them with more effective medication, and free treatment. Prevention trials could also take unfair advantage of the reality that female sex workers (and injecting drug users) engage in behaviors which put them at a higher risk of becoming HIV infected, and that they may be incapable to use “prevention packages”. However, just because high-risk women’s circumstances may be considered unjust, does not necessarily pursue that a possible transaction between researchers and high-risk women might be exploitative. The research findings could, on the other hand, reveal that there is a possibility that the distribution of the level of potential benefits might be unfair, in transactions which might involve Cambodian high-risk women and researchers (as regards to HIV trials). Consequently, in accordance to the Wertheimerian concept of exploitation, it is found to be an increased risk that prevention trials, involving high-risk women in Cambodia, might be exploitative. In conclusion, totally four risk indicators (out of four) signify that there is an increased risk of exploitation. It is therefore, according to the risk assessment tool, finally estimated that Cambodian high-risk women are at great risk of being exploited as research participants in HIV trials.
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