Risk, Rewards and Regulation:

Exploring Regulatory and Ethical Dimensions of Human Research Participation in Phase I (First-in-Human) Clinical Trials in The United Kingdom

SHADRECK MWALE

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Declaration

I hereby declare that this thesis has not been submitted, either in the same or different form to this or any other University for a degree.

SUMMARY

University of Sussex

SHADRECK MWALE
DOCTOR OF PHILOSOPHY

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In recent years, contemporary society – particularly in the West – has witnessed a growth in the production, promotion and consumption of pharmaceutical products, particularly for disease treatment. The process of producing these medicinal products involves testing for safety and efficacy on, among others, healthy human subjects. Taking a phenomenological approach, this thesis examines how risks, rewards and regulation associated with first-in-human clinical trials (FIHCTs) are viewed and experienced by regulatory and corporate professionals, and by healthy volunteers. Using conceptual and empirical forms of inquiry, the study shows how current understandings of human involvement in clinical trials heavily influenced by bioethical conceptions of healthy volunteers as rational, altruist and willing participants, limits our appreciation of the context in which such acts take place. This is because the decision to take part in trials is shaped by the situation in which people find themselves. Appeals to rationality, altruism and voluntarism do not explain all the elements that go into that decision. Therefore, new insights into the lives of healthy volunteers challenge bioethical conceptions and generate new frameworks for policy and practice of FIHCTs.

Having identified a gap in medical sociology research on healthy volunteering in FIHCTs in the UK, this qualitative research project brings the findings of extensive desk and field research into analytical discussion. Specifically the research examines existing regulatory discourse and practices around the implementation and conduct of clinical trials and experiences of healthy volunteers in clinical trials in the UK. It investigates how the different actors view and experience the risks that emanate from medical technological innovations, and how their views shape human involvement in drug testing. Data were gathered from documentary analysis, interviews with 4 corporate professionals, 8 regulatory officials and 35 healthy volunteers, and a survey of 187 healthy volunteers.

This research breaks ground for further social scientific research into healthy volunteering in FIHCTs in the UK. Specifically it adds to calls for more nuanced discussions of human involvement in clinical trials and the unpacking of concepts such as "volunteer", "compensation" and "informed consent" in clinical trial contexts. Schutz's (1970) "system of relevance" is used as a tool for studying the interaction of risk, rewards and motivation for both the "individual" and the "institution". The findings show that the existing regulatory system is fragmented, and healthy volunteers are often pushed to the margins of the regulatory system. In

addition, regarding participants in clinical trials as "willing volunteers" serves to obscure the ways in which inequality is perpetuated and experienced by some participants in these early studies. The thesis concludes by suggesting that Schutz's system of relevances offers a valuable insight into the study of healthy volunteering.

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Acronyms

ABPI	Association of the British Pharmaceutical Industry
CCRU	Common Cold Research Unit
CHMP	Committee for Medicinal Products for Human Use
CIOMS	Council for International Organizations for Medical Sciences
CRO	Contract Research Organisation
CRF	Clinical Research Facility
CTD	Clinical Trial Directive
CTIMP	Clinical Trials of Investigational Medicinal Products
DoH	Department of Health
EMA	European Medicines Agency
EU	European Union
FIHCTs	First in-Human Clinical Trials
FOI	Freedom of Information
GCP	Good Clinical Practice
HRA	Health Research Authority
HPV	Human PapillomaVirus
HV	Healthy Volunteer
ICH	International Conference for the Harmonization
IMP	Investigational Medicinal Product
MHRA	Medicines and Healthcare products Regulatory Agency
NREAP	National Research Ethics Advisory Panels
NRES	National Research Ethics Service
NVR	National Volunteer Register
ONS	Office of National Statistics
REC	Research Ethics Committee

RES	Research Ethics Service
TGR	The Gift Relationship
TOPS	The over-volunteering prevention System
VIP	Volunteer Inclusion Period
VRB	Fichier National/Volontaires Recherches Biomediclaes
WHO	World Health Organisation

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Chapter 1
Introduction

1.0 Research journey

My interest in the subject of this research started in March 2006 during in a conversation with a colleague, Christina Ryan, about the novel "The Constant Gardener" by John Le Carre. The novel tells the story of a British diplomat, Justin Quayle, who meets an activist, Tessa, marries her at her request and takes her on a diplomatic mission to Kenya. Tessa is murdered. Justin decides to investigate her death against the strong wish of his superiors to let the matter quietly disappear. He discovers secrets involving members of the British High Commission and the sleazy business practices of the multi-billion-dollar pharmaceutical industry (LeCarre 2006). My colleague and I, reacting to the portrayed disregard that the pharmaceutical corporations and politicians had for human life, began to discuss how social research on pharmaceuticals and society should be carried out.

Soon after, I learned of the Northwick Park incident in London late in March 2006 in which healthy volunteers in a phase I clinical trial for a cancer drug TGN1412 suffered severe effects while taking part in the trial (Sample and Maley 2006). This incident aroused public disquiet over the safety of phase I trials and the ethics of pharmaceutical corporations in administering such trials. However, despite the outrage by the public, media reports noted an increase in the number of people willing to take part in clinical trials (Mckie and Revill 2006). These events led to a series of discussions with my colleague about the ways in which pharmaceutical corporations are regulated and what could be done to research their practices. After a series of meetings with potential supervisors and bouncing ideas off my colleague, this project was born.

1.1 Rationale and context of the research

The objective of this research is to explore ways in which the risks, rewards and regulation of phase I clinical trials that specifically involve

healthy volunteers are viewed by professionals, regulatory bodies and lay volunteers in these trials. The study explores how risks arising from medico-technological innovation and testing are perceived and experienced across commercial and social spaces within the UK, and to consider whether existing ethical and regulatory structures and standards governing the protection of clinical research subjects in the UK offer equal and adequate protection to UK citizens in diverse social circumstances. The thesis describes the organisation and structure of regulation of first-in-human clinical trials (FIHCTs) in the UK, and explores questions about the biographies and motivations of healthy volunteers and their understanding of risks associated with FIHCT research. It asks what role financial rewards should play in FIHCTs, how such rewards are regulated, and what their impact is on the ethical conduct of these trials. Lastly, it investigates how the UK political, commercial and healthcare institutions influence the practice and implementation of FIHCTs and European Union guidelines respectively.

This chapter gives an outline of the research on which this thesis is based. It first states the context, then gives a brief discussion of the history of human involvement in clinical trials and the emergence of volunteering as a prerequisite, and goes on to describe the commercial context of the study: the growth of the pharmaceutical industry and the consequent growth in demand for healthy volunteers. Linked to this is a discussion of the regulatory context which considers how regulatory changes, specifically the implementation of the Nuremberg Code, have contributed to a shift from the use of captive and vulnerable individuals to encouraging the use of people capable of "voluntary" and "rational" consent. Then follows a discussion of the substantive focus of the study – what clinical trials consist of and how FIHCTs are organised and regulated today. The chapter concludes with a discussion of the contribution the study makes to sociology and provides an outline of the thesis as a whole.

1.2 Context of human involvement in clinical trials

Until approximately one hundred years ago, the production and use of medicines for humans was both uncontrolled and unconventional (Carter 1995; Bartifai and Lees 2006). The development of the pharmaceutical industry as we know it today has its roots in major pharmacological developments and scientific breakthroughs that occurred before and after World War II, when antibiotics such as penicillin, streptomycin and several other broad-spectrum antibiotics were discovered and mass-produced (Petryna and Kleinman 2007:2). Though drugs have been tested on people far before the 18th century, the systematic testing of drugs on humans is a recent phenomenon, and is connected to the rise of drug regulation regimes and controls on how drugs can be administered (Bartifai and Lees 2006). Before the rise of drug regulation mechanisms, drugs were often tested haphazardly on patients who were mostly poor people or slaves; some of these practices continued even when a systematic procedure of drug testing developed in the 20th century. In the United States, testing was carried out on prisoners and in the UK on patients and army service personnel who served as human guinea pigs (Rosner 1996; Bolton 2005). Although tests had been done on humans prior to the 20th century, it was during the first four decades of the 20th century (Marks 2009) that scientists started to test drugs systematically on a select few individuals in randomised clinical trials. The origin of randomised clinical trials can be traced to the Elixir Sulfanilamide tragedy of 1937[1] (Carpenter 2010). Before then, and in the UK up until the 1960s, drug developers were under no obligation to test or to demonstrate the safety of their drugs before marketing or public use. The tragedy aroused widespread public disquiet over the safety of drugs. The Food and Drug Administration (FDA), itself trying to establish itself as a force in regulating the industry at the time, conducted an extensive investigation, which identified the lack of

[1] *In 1937 a doctor in Tulsa USA developed Elixir Sulfanilamide, as part of what was then a growing trend in the use of sulfanilamides in Europe in the treatment of common colds. However, Elixir Sulfanilamide itself was actually diethlene glycol – a highly toxic substance similar to ingredients found in anti-freeze and was sold as an infective treatment for venereal diseases. People who consumed this drug become seriously ill and at least seventy-three people died. Following extensive media coverage, the Food and Drug Administration (FDA) concluded that drugs should be tested before being put on the market.*

pre-marketing testing as a problem of the process that resulted in the disaster. Therefore, on December 1, 1937, an amendment was added to legislation that required drug manufacturers to provide "records of their clinical and non-clinical experiments" before drugs would be certified for public sale or use (Carpenter 2010:103). However, in the UK it was not until 1968 that systematic pre-marketing testing of drugs was instituted. At the time such testing was voluntary (Rägo and Santoso 2008).

Research focus: what are clinical trials?

This research explores human involvement in FIHCTs. Clinical trials involve a set of practices that are required before new drug molecules can be declared safe and effective for marketing. The clinical trial process today is involved and elaborate, relatively standardised across the world and is carried out in a "number of stages, contributing to the immense time, risk and expense of the drug development process" (Rajan 2006:67). First, the drug is put through pre-clinical tests for toxicity. This usually involves conducting tests on animals in order to establish if the new molecule is safe to introduce into humans (Pocock 2000). If a molecule is deemed too toxic, it does not proceed to the next stage; if considered sufficiently safe, it proceeds to clinical trials, which often involves four stages, starting with the first-in-human phase.

My research focuses on phase I (first-in-human) clinical trials. These trials are carried out on a limited number of healthy volunteers with the aim of testing the basic safety of the drug and to determine the maximum dose that can be administered without causing serious harm. The participants in this phase usually have no health benefits to gain from their involvement in these trials (Elliott and Abadie 2008; Goldacre 2012). I should point out here that the moniker "phase I clinical trials" is also often used generally to refer to clinical trials that involve healthy participants on trials testing IMPs that are already on the market. In addition, some phase I trials are also conducted on patients, particularly for developing cancer and HIV/AIDS drugs (Kohli-Laven et al. 2011). This is because, strictly speaking, it is deemed unethical to expose healthy subjects to drugs which are highly likely to be toxic to humans, although there are

cases where such drugs have been tested on healthy subjects (Gupta et al 2012; Andrew and Roy 2004; Dagher 2005; Guideline IHT 2009). Phase 2 involves a larger numbers of patients and aims to investigate further the efficacy and refining of optimal doses. This involves patients in controlled numbers and holds no obvious benefits for participating patients (Pocock 2000). Phase 3 clinical trials involve samples of several thousand participants who are usually suffering from the very disease for which the new drug has been developed. During phase 3 the drug continues to be tested for safety and its therapeutic benefits are evaluated. The fourth phase aims at comparing existing remedies with the new drug and establishing how treatment might work in a broad range of patients (Kerr et al. 2006). Most drug compounds do not proceed beyond phase I due to their toxicity. The process of taking a drug from the laboratory to a hospital or market is an arduous one. It takes between 10 and 15 years. Estimation of the real costs involved in this process is equally difficult (Abadie 2010). However, the process has become increasingly contentious as the public calls for cheaper drugs, arguing that production costs are low and that the market value that companies attach to the finished product is not justifiable (Abadie 2010). Recently, phase I clinical trials have attracted public criticism – the Northwick Park incident of 2006, in which six healthy volunteers suffered severe side effects after taking part in a phase I trial for the cancer drug TGN 1412 (MHRA 2006), led many people to claim that the trial had been conducted amid open disregard for safety and regulation. Others called for tighter British regulation of the pharmaceutical industry, claiming that it favoured corporate interests over the safety and interests of participants (Stebbings et al. 2009). However, healthy volunteer involvement in clinical trials is not a new phenomenon. In the following section, I will give a brief account of the advent of mass healthy volunteering.

The beginning of mass healthy volunteering

The term "volunteer" is not commonly discussed within sociology. In its daily use volunteering tends to carry connotations of willingness, help and selflessness without prospect of payment. The term has long been

open to interpretation, but, in general, it can be seen as doing something without expecting a reward; it is seen as proactive rather reactive (Wilson 2000). For instance, among people in full-time employment, volunteering for a charity is seen as a commendable thing to do. Bolton (2005), a historian, observes that in the UK the term "volunteer" is associated with the enlistment of soldiers during the world wars as the ultimate demonstration of courage and selflessness. Bolton argues that today volunteering seems to carry similarly loaded meanings. However, in the 1950s, particularly within the army, to "volunteer" came to be associated not only with a personal decision to enlist but also as an expectation of service personnel to do certain things when asked and whenever the need arose. Bolton (1995) illustrates the historical complexity of the term by citing an incident at the birth of the Common Cold Research Unit (CCRU) in the 1950s, when the management of the unit and at the Ministry of Health at the time wanted to define the term "volunteer". In this exchange, the then Health Minister expressed concern over the use of prisoners and service personnel, considering them incapable of "volunteering". Of interest here is how even during the 1950s there was an indication that officials were against the use of people for who were not, strictly speaking, able to free agree to participate in medical research because of the institutional context.

Within sociology, the term "volunteer" has also been contested. Wilson and Musick (1999) argue that volunteering can be informal or formal and can include productive work that should be recognised as requiring both social and cultural capital (Bourdieu 2005) to function; it should thus be rewarded. However, the reward here is not clearly defined; it could take the form of either money or non-monetary rewards, such as encouragement or acknowledgement. Wilson (2000) argues that there is no consensus on the meaning of "volunteering" but that it can be linked to the giving of time freely to benefit others and is among a cluster of helping behaviours. Other discussions in sociology about volunteering revolve around questions of motives, rationality, rewards and altruism (Wuthnow 1993; Weber, Swindler and Parsons 1963). However, less attention has been paid to the context in which volunteering takes place and how

volunteering takes on different meanings depending on social circumstances.

At an individual level two theories of volunteering can be distinguished. The first considers the individual as complex and multi-dimensional and located within a given context and background. This theory perceives volunteering subjectively and it emanates from sociological attempts to investigate motives for volunteering. The second theory assumes individuals are motivated by simple mechanisms; it considers the context in which decisions are made as complex, and is more behaviourist in orientation. This view also considers actors as rational so that accounts of volunteering are based on a cost-benefit analysis (Wilson 2000). In this research I have used a subjective approach to volunteering to consider not only the role of rewards and individual rationality but also how to demonstrate the conflicts and complexity of individuals as social actors and social situations, and how these determine and define acts of voluntarism in society.

Volunteering in clinical trials

Human involvement in clinical trials has not always been based on volunteering. As mentioned in the first section of this chapter, human involvement in clinical trials was often a result of the use of force against mostly captive populations. Historians Hazelgrove (2002), Bolton (2005) and Washington (2006) and the sociologist Epstein (2004) attest to the fact that prisoners and ethnic minorities were often coerced into participating in clinical trials. Growing objections eventually led to the development of the 1946 Nuremberg Code, which followed the revelations of grossly unethical research experiments in Nazi Germany in the 1940s. The Nuremberg ruling on human involvement in clinical trials was a set of ethical codes of practice aimed at curbing the abuse of human subjects (Scocoza 1989; Bartifai and Lees 2006; Abadie 2010).

However, in many countries, including the UK and the US, the Nuremberg Code was largely disregarded (Bolton 2005). For instance, during the 1950s and 1960s, the use of servicemen and women as research

subjects in the UK was common and so were cases of abuse, and of trials going badly wrong. For instance, the death in May 1953 of Airman Ronald Maddison at Porton Down chemical research facility in Salisbury in the UK after being exposed to nerve gas was in 2004 ruled an unlawful killing (Bolton 2005). In the US, it was not until the 1980s that the use of prisoners for medical research was officially outlawed (Goldacre 2012). Hazelgrove (2002) argues that the actions of Britain at the time of the Nuremberg Code served to divert attention away from its own unethical practices while ensuring the protection of professional power to carry out research. Reports by medical practitioners such as Goldby (1959) and Pappworth (1967) exposed unethical practices in British hospital trials involving patients. During this period, self-experimentation was also common as researchers or staff in laboratories took part in their own studies. However, questions about risks and ethics are different when students in laboratories or patients in hospitals are asked by their lecturers and doctors to take part in clinical trials. Here influence and power come into play as fears of letting superiors down may influence an individual's perception of risk and involvement in clinical trials (Goldacre 2012). The question of how pressure to comply might influence human behaviour can be seen in Milgram's psychological experiments in which force or the need to obey those in authority was clearly demonstrated as a factor in human behaviour (Milgram 1959).

Changes in attitudes about ethical approaches to medical research were brought about partly by the thalidomide and Tuskegee scandals and the growth of the civil rights and anti-apartheid campaigns of the 1960s and 1970s, which protested the abuse of ethnic minorities (Abadie 2010; Hazelgrove 2002). In the Tuskegee incident in the US, over 500 black men suffering from syphilis were unknowingly recruited into a study of the disease and denied treatment (Des Jarlais and Stepherson 1991). The use of thalidomide to alleviate morning sickness in pregnant women resulted in the birth of infants with malformations in Western Europe and North America. These scandals caused growing public disquiet regarding the conduct and regulation of clinical trials. As a result, during the early 1970s, human involvement in clinical trials came to be portrayed as a social good,

with images of people engaged in leisure activities during trials (Bolton 2011). The Belmont report, published in 1979, has since shaped bioethics practice and discourse (DHEW 1978). Moreover, changes to funding following the economic downturn of the 1970s meant that by the early 1980s there was an increase in clinical trials as drug development was privatised (Mirowski and Van Horn 2005), resulting in further growth of the industry. Developments in science, which led to a better understanding of the biology of the human body and its interactions with chemical agents, brought about further change. Clinical trials became established as a standard for the testing and certification of the safety and efficacy of new drugs, governed by ethical codes and driven by the need to mass-produce antibiotics and other profitable drugs. Gradually, clinical trials became a highly successful business and pharmaceutical companies such as Pfizer (Marks 2009) and other organisations expanded, including contract research organisations (CROs) which conduct clinical trials on behalf of pharmaceutical companies. However, restrictions and regulation governing the recruitment of volunteers meant that readily available participants – for instance prisoners – were no longer accessible (Abadie 2010). Instead, pharmaceutical companies had to depend on willing members of the public. In addition, the growing pressure to quickly develop commercially profitable drugs (Illich 1995) led to an increase in the demand for human volunteers on whom these drugs had to be tested. This meant that human bodies became highly valuable resources for pharmaceutical companies, as scientists reconceptualised their objects of study "not as a people but as a population" which could be brokered as valuable research subjects in the commercial pharmaceutical context (Petryna 2005:3).

It was during this period that incentives to encourage participation were introduced which are still recognisable today. Incentives in healthy volunteering could be seen in experiments at Porton Down, where it was argued that some kind of incentive was needed to ensure wider involvement. Until 1955, service personnel who took part in studies at Porton Down were paid the sum of one shilling for risking their lives and health. But the Treasury was willing to increase the reward when the matter of extra pay was raised with the Treasury in a letter of October 17,

1955, by P.L. Burton of the War Office, in which he gave an overview of the history of the payment of "servicemen volunteers" (Bolton 2005:8). The rationale was that the tests were dangerous and unpleasant and that the payment of one shilling was not sufficient incentive. Staff running the clinical trial unit asked that payment be increased because of the dangerous and unpleasant nature of the "work". Though payment was increased, it was discussed only in relation to service personnel at Porton Down, and there is no evidence that healthy volunteers involved in trials in other medical research were paid (Bolton 2005).

1.3 Commercial context

In the UK, US and other Western countries, clinical trials began to take place on a large scale from the 1970s and pharmaceutical companies became a major source of tax revenue (Bartfai and Lees 2006). The evolution of the pharmaceutical industry as a profitable, successful business since the 1970s brought an increase in the demand for human subjects to take part in clinical trials. This has extended beyond national boundaries, with many clinical trials now moving offshore to poor and developing economies. The anthropologist Petryna (2005:2) observes that clinical trials are migrating "globally to so-called non-traditional research countries experiencing demographic change associated with declining health resources but having little or no share in the global pharmaceutical market".

By 2001 it was estimated that there were about 10,000 clinical trials taking place worldwide (Petryna 2005:2). By July 2013 about 172,178 clinical trials were taking place worldwide (US National Institute of Health), but this refers only to those registered with a clinical trials portal. This significant increase in the numbers of clinical trials conducted offshore is thought to be a result of the growing number of trials taking place every year, making volunteer numbers insufficient in the West. It is also thought that the need to meet regulatory requirements has contributed to this increase, for example in the US, where large numbers of participants are required before a drug is certified as fit for human use. On

the other hand, calls by the International Conference on Harmonisation (ICH) for the creation of international regulations aided the growth of offshoring as the ICH allowed for the transfer of clinical data from international studies to the Food and Drug Administration (FDA) of the US for approval of new drugs (Petryna 2005). Recently the UK government has tried to bring about collaboration between pharmaceutical companies and the National Health Service (NHS) in later-phase trials, not only for the benefit of science but also with the stated aim to "improve" care within the NHS, clearly raising ethical (and sociological) concerns about the tensions between research and healthcare (Will 2011). The later-phase trials that are the subject of the proposed collaboration are often seen as part of the improvement of care in pioneering research and also as a part of care for patients with conditions for whom existing treatments may not have worked. Early phase trials are not part of this collaboration; most of them are conducted offshore.

The global offshoring of clinical trials is also influenced by the complex needs and healthcare situations in emerging economies. Reduced government funding for research and healthcare in these countries leaves local scientists and lay people open to taking part in these trials so as to advance science or have access to healthcare (Rajan 2006). Thus scientists in these countries actively seek to establish contacts with CROs, hoping to host clinical trials (Petryna 2005). However, despite the growth in offshoring, the pharmaceutical industry is still very strong in the UK.

According to the Office of National Statistics (ONS), the pharmaceutical industry contributes about three times the size of the textile and clothing industry to the UK economy (ONS 2014; Towse 1996; Abraham 2008; Abraham and Lewis 2000). With regard to the size of the pharmaceutical industry, as of January 2015 the Association of British Pharmaceutical Industry (ABPI), an influential organisation that lobbies the government and the EU on behalf of its members (Abraham and Lewis 2000), had approximately 51 pharmaceutical companies and CROs registered as members (ABPI 2014). This number does not reflect the total number of companies operating in the UK, as membership of the ABPI is

not mandatory. Furthermore, some of the larger pharmaceutical companies conduct some phase I trials on their own while some – especially small and upcoming pharmaceutical companies – contract out such trials to CROs to cut costs. With regard to CROs registered to conduct FIHCTs in the UK, by November 2014, there were about 15 clinical trials units accredited as part of the MHRA Phase I accreditation scheme aimed at licencing CROs to conduct FIHCTs (MHRA 2014a). Under this scheme, which developed following the Northwick Park incident, CROs are only permitted to conduct a FIHCT if they are accredited having met certain set criteria. Among the criteria is the need to have a Principal Investigator who has a qualification in conducting FIHCT (MHRA 2014b).

With regard to the recruitment of health volunteers, CROs advertise in newspapers and on their websites. The CROs call for interested individuals to register their interest, after which they are sent regular information as and when screening for trial commences. Figures 1.1 and 1.2 below are examples of advertisements.

Figure 1.1: Example Excerpts of CRO Advertisements

Source: https://www.quintilesclinicaltrials.co.uk

In the above advert, it is interesting to note the way in which altruism is invoked – asking volunteers to come forward to contribute to the development of medical research, which benefits the wider population. In this case, volunteering is framed as moral and a social good. Attention should also be paid to the emphasis on how significant volunteers are

thought to be to the research process by stating that "…volunteers are key to the success of the research". Such advertisements are common in some open calls for volunteers to register their interest in participation. Figure 1.2 below, however, shows a call for volunteers both to a specific trial and a general message to anyone interested in taking part in clinical trials.

Figure 1.2: Example Excerpts of CRO Advertisement

Source: http://www.londontrials.com accessed 18/02/2015

What is of interest here is how in this specific call to enrol into specific clinical trials there is emphasis on the personal benefits healthy volunteers will obtain in the form of a financial reward. Similarly, the call for general enrolment seen here in the lower right corner of figure 1.2 also alludes to the financial rewards available and how easy it is to become a "paid volunteer". On the other general call in the bottom left corner of figure 1.2, while attempting to explain how drugs are developed, focus quickly shifts to portraying taking part in clinical trials as a comfortable and relaxed experience akin to taking a holiday. In summary, the advertisements invoke altruism and rewards to healthy volunteers for

taking part in clinical trials; they make no reference to the risks associated with taking part in clinical trials.

CROs specialise in locating research sites, recruiting participants as illustrated above, and sometimes drafting the design and analysis of the study. The clients of CROs are pharmaceutical companies who contract them because they are seen as efficient, quick and cheaper than the traditional academic institutions that used to carry out these functions (Petryna 2005). The role of biotechnology or pharmaceutical companies is to sponsor the clinical trials, while the CROs organise the trials in multiple centres, increasingly on a global scale. For far less invasive or less risky clinical trials, universities and other publicly funded institutions are used. However, although universities and other publicly funded laboratories continue to carry out low-risk studies and to play a major role in the development of drugs (identifying potential lead molecules, for example), the work required for the licensing of potentially good molecules tends to be given to CROs. Consequently, the biomedical and experimental rationales for clinical trials become interwoven with the market potential that these companies hope for, together with the risks inherent in the drug development process (Abraham 1997; Rajan 2007). This situation has fostered a collaborative relationship between corporations and universities. Though universities are key in identifying lead molecules, there are also times when corporations have funded studies in universities, blurring the private versus public research divide (Petryna 2009). The types of clinical trials that take place in universities are on a very small scale and are subject to scrutiny by internal ethics committees. These studies are also considered less risky because if human subjects are involved the trials are non-invasive. However, although studies in academic settings are usually deemed low-risk, they are not always free of controversy. In July 2002 a healthy volunteer died in the US after taking part in a study aimed at investigating the reflex that protects the lungs of healthy people against asthma attacks. She was made to inhale hexamenthonium, a substance once used to treat high blood pressure; afterwards she developed a cough, her condition worsened and she died (Savulescu and Spriggs 2002). This highlights the complexity in risk considerations associated with FIHCT

studies. In some cases what might be deemed low risk and fit for "relaxed" regulation might in fact be as risky as so-called high risk studies. The following section examines the regulatory context and responses to what became known as the Northwick Park incident.

1.4 Regulatory context

Clinical trials have had a troubled history associated with scandals and fatalities as can be seen in the incidents cited above. On the one hand we have pharmaceutical companies who want to make profits, albeit with governments regulating them, and on the other hand the public wants safe drugs, healthy lives, and for science to make the world a safer and better place (Bartfai and Lees 2006).

From an economic point of view, regulation can be construed as state intervention in the market (Abraham and Lewis 2000), including oversight of contracts and ownership rights so central to transactions in capitalist economies. However, the distinction between the market and regulation is not quite as clear as it is made out to be by free-market advocates. Rather, regulation may be useful in both creating and demarcating how far markets can go (Scott 2004; Abraham and Lewis 2000). By being involved in this way, the state's actions impact the interests of industry and consumers (Majone 1994; Ünay 2013), but state involvement in healthcare markets – unlike that in consumer markets – is strongly linked to the state's responsibility for the safety of its citizens.

Over time the Nuremberg Code, described earlier in this chapter, has been updated in response to criticism, for instance, that it failed to take into account the context in which the trials were done. It was replaced by the Helsinki Declaration in 1964 (Scocozza 1989), which also sought to advance the protection of volunteers in medical research. However, like the Nuremberg Code, the Helsinki Declaration was the target of much criticism, notably for its failure to provide adequate protection for participants. Media reports at the time exposed a number of serious breaches of ethical guidelines. Pappworth's persistent publication of reports about experiments involving vulnerable patients and captive groups

in 1967 in British hospitals, for instance, showed how the Nuremberg Code and the Helsinki Declaration were ignored in Britain. Other reports pointed to the Tuskegee incident. Thus it has been argued that researchers in the US and Britain not only ignored the Nuremberg Code on informed consent but deceived the world by strongly condemning the original Nuremberg experiments in order to divert attention from unethical practices in their own countries (Hazelgrove 2002). Other studies highlighted differences in interpretations of what was meant by "ethical" practices. As a result, the Helsinki Declaration was amended in 1975 at a medical conference in Tokyo, leading to a second declaration (Scocozza 1989). The revised version is still in force today, though it had gone through a further four revisions by 2000 (Vastag 2000). The Helsinki Declaration stipulates that a research protocol with clearly explained plans and procedures must be made available to established ethical committees for analysis and guidance before any research is conducted; for non-therapeutic biomedical research the participants must be volunteers for whom the trial will have no health benefit. Today many ethical and policy guidelines, including those of the EU on clinical trials, have built on these initial guidelines (EMEA 2007). Nevertheless, some critics feel the declaration is an outdated guide and question whether continued revisions of the initial declaration affect its relevance in terms of practical implementation (Vastag 2000).

Within the EU different national, supra-national and international guidelines are now in place to oversee the protection of human volunteers' rights, safety and wellbeing during the various phases of clinical trials. The guidelines are the same for all four phases of the clinical trials and are enforced by competent national authorities (Abraham and Lewis 2000). However, as recently as 2006 in several EU member states such as Germany, the UK and the Czech Republic, there was no strict enforcement of the regulation requiring investigators to submit applications to regulators before conducting clinical trials. Instead, trial applications were often hastily processed with little independent ethical review (Marshall and Castle 2007; Hedgecoe 2013), despite the fact that phase I clinical trials are the riskiest in the clinical trial process – the first

time that drugs are tested on humans to assess levels of toxicity and ascertain safety (Elliot and Abadie 2008). However, following the Northwick Park incident, the EU regulator, the European Medicines Agency (EMA), was compelled to issue new guidance to ensure strict controls over the conduct of the FIHCTs. In the latest guideline, the EMA emphasises that it is required during clinical trials that the rights, safety, and wellbeing of the trial volunteer participants must prevail over interests of science and society (EMA 2007).

Analysis of these guidelines, discussed at length in Chapter 4, shows that the EMA guidelines do not mention the role of monetary inducements in FIHCTs or how they are to be calculated or regulated in practice. Despite this regulatory oversight, in the bioethics literature there has been a growing debate on the role of monetary rewards in FIHCTs. Hale (2007) and Elliot and Abadie (2008), among others, argue that the role of inducements cannot be ignored in ethical considerations of clinical trials since inducements clearly affect people's judgment about whether or not to participate in clinical trials.

History of the European Clinical Trials Directive

It should first be noted that the process described here cuts across the period of the data collection of this research. Preceding the introduction of the European Clinical Trials Directive 2001/20/EC (CTD) on May 1, 2004, clinical trials in the UK were governed by the Medicines Act of 1968. For UK clinical trials in patients, Clinical Trial Certificates (CTCs) had to be obtained; this was the case until 1981 when the Clinical Trial Exemption/Doctor and Dentist Exemption (CTX/DDX) system was introduced. At the same time, it should be noted that before May 1, 2004, there were variances in approval procedures and laws relating to the conduct of clinical trials within the EU (EU parliament 2001; Hedgecoe et al 2006; Hedgecoe 2012).

The main concern of the EU at the time when changing regulation was to protect and sustain the EU clinical trials market. More precisely, the purpose of the European CTD was to develop an increasingly harmonised

and simplified approach to the conduct and regulation of all clinical trials carried out within the EU (Hartmann 2012; Abraham and Lewis 2000). The EU member states were expected to adopt and publish national legislation and administrative provisions necessary for compliance with the European CTD before May 1, 2003, and had to apply these provisions at the latest with effect from May 1, 2004. In the UK, these requirements were achieved through UK Statutory Instrument 2004/1031 the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 1031). Statutory Instrument 2004/1031 outlines the procedures for both regulatory and ethical assessment of all clinical trials including those on IMPs in order to obtain a Clinical Trial Authorisation (CTA). In addition, the statutory instrument sets out standards by which trials should be conducted (Good Clinical Practice, [GCP]) and provides the basis for powers to regulate clinical trials, such as inspection and enforcement (Medicines for Human Use [Clinical Trials] Regulation 2004).

While the development of the directive that resulted in the 2004 regulatory changes to clinical trials could be taken in the wider context of policy and science debates following, for instance, the outbreak of Bovine Spongiform Encephalophathy (BSE) in the UK (Brown 1998; Taylor 2003) and debates about the safety of genetically modified foods that emerged in the late 1980's through to today and their impact on general public's trust of science, there seems to be no clear link between these events and the changes that led to the 2004 Medicines for Human Use (Clinical trials) Regulation. Rather evidence so far seems to point to the EU harmonisation agenda as outlined above. As an illustration of EU policy-making practices driven by internal EU interests, the 2001 CTD directive has recently been revised. The new directive, which came into effect in October 2014, was reviewed following an announcement by the EU commission in December 2008. The review aimed to assess options for improving the functioning of the European CTD with a view to making legislative proposals, if necessary, within the context of the global market for clinical trials. A public consultation was carried out during the latter part of 2009, and, as a result, a concept paper on the revision of the European CTD was published and a second public consultation began in

February 2011. The concept paper specifically sought to investigate two significant disadvantages of the 2001 European CTD. First, it looked at the impact (of what was seen as unnecessary administrative costs) of the requirement that largely identical information be shared and sent to several different member states when applying for clinical trial permits. Secondly, the assessment was meant to explore whether the requirements set out in the European CTD were being applied differently in different member states. While the broad concepts of the CTD are identical, divergent and conflicting points of view could surface when dealing with the details of the request for a CTA in different member states (EU commission 2011). Different options are currently being explored by the European Commission to address these disadvantages.

As can be seen from the preceding discussion, the motivations and aims of the European CTD are therefore to ensure the facilitation of the internal EU market by eliminating barriers to clinical research and building a harmonised and more efficient process for the conduct of European clinical trials. To achieve this objective, clinical trials taking place in multiple states should become simpler to carry out and more cost-effective. In addition, the EU CTD also provides a framework for a consistent regulatory compliance to GCP in relation to the protection of clinical trial participants (whether as patients or healthy volunteers). The CTD also sets the standards of and frameworks for improvement of the data from clinical trials conducted in all member states, by setting standards of its robustness and reliability (EU Commission 2011).

Implications of CTD on UK clinical trials

The major change in the clinical trials process in UK clinical research after the implementation of the 2004 Medicines for Human Use (clinical trials) Regulation, was first that the authorisation became an authorisation for the clinical trial itself, i.e. a CTA. The previous legislation derived from the Medicines Act of 1968 controlled the supply of the drug product. Second, the introduction of the European CTD on UK clinical trials meant that the legislation would now cover both patient and healthy volunteer studies. Prior to May 1, 2004, healthy volunteer studies or

FIHCTs were not included in the regulation of clinical trials. The inclusion of FIHCTs in this regulation was concerning for the industry as they saw it as potential barrier to clinical research in the UK, and there were industry concerns that pharmaceutical companies would move such studies to countries with less regulation and where the approval process would be faster (Abraham 2007). Today, in practice the timescale for the initial assessment of FIHCT applications is generally said to be 14 days from the receipt of a valid application. According to the MHRA the concerns over the delayed approval process from industry have diminished since May 1, 2004, but whether this view is shared by the industry remains to be seen.

Other implications of the European CTD on UK clinical trials include the introduction of the manufacturing/importation authorisations for companies involved in the manufacture and/or importation of Investigation Medicinal Products (IMPs). There is also a requirement for the Qualified Person (QP) based at the importation site to make a declaration regarding GMP standards at any non-EU manufacturing site. Other changes saw the introduction of a statutory basis for Ethics Committees as part of the structured regulatory system and the establishing of inspection and enforcement powers by regulatory bodies – in this case the MHRA (Medicines for Human Use Regulation 2004).

Politics and regulation of clinical trials

Regulatory frameworks do not exist in a vacuum. They emerge from political and commercial landscapes in which the implementation of guidelines is influenced by both national and international political and commercial interests (Daemmrich 2004). As a result, the pharmaceutical industry often finds itself caught between international and national politics as governments and players such as activist groups contend over the protection of their interests. At the international level, economic interests (Rajan 2006), security and safety are at stake, as shown during the pandemics of swine flu in 2009 and the pathogenic avian flu, H5N1 (Elbe 2010; Davies 2008; Herington 2010), and the global response seen in increasing surveillance and government expenditure on treatments such as Tamiflu. At the micro or local level, political action is urged regarding

citizens' health, with public health and patient group organisations demanding greater representation and influence in pharmaceutical innovations (Daemmrich 2004).

These political contexts and interests further shape the relationship between the state, the industry and the public. In the global market economy, it is inevitable that tensions will arise between the need to promote industry and foster competition while ensuring that commercial liberties are not abused. Regulation comes into play as governments attempt to manage these conflicting interests. As mentioned in the foregoing section, the regulation of FIHCTs are not particularly different from the regulation of other phases of trials. Like all clinical trials, FIHCTs are subject to a hierarchy of governance structures and processes ranging from international bodies such as the World Health Organisation (WHO) and EMA to local research ethics committees. For all trials, safety checks start in the laboratory with animal testing and are carried out all the way through the later phases of development to post-marketing checks. With regard to FIHCTs, regulation is imperative as the trials and ultimately the drugs developed affect both volunteer and patient health in terms of benefits and potential risks. However, the ways in which pharmaceutical regulation is organised and conducted in market economies is exceedingly contentious (Abraham and Lewis 2000). Hedgecoe's (2013) study of regulatory practices examines how concerns about the over-regulation of the pharmaceutical industry in the 1980s emerged in response to the economic downturn of the 1970s and resulted in the introduction of the clinical trial exemption scheme, which led to a less rigorous review of trial procedures. Hedgecoe argues that this response to foster industry growth was part of regulatory practice until 2004 when there was a change in regulation, but in 2006 such relaxed attitudes to clinical trial reviews were still common. For FIHCTs, concerns about state regulation inhibiting industrial growth are common, as are issues to do with protecting individuals who volunteer in trials. It is how such attitudes relate to FIHCTs that this thesis aims to explore.

1.5 Sociological contributions

To date there has been no research in the UK solely to identify how healthy volunteering takes place; as mentioned earlier, most research has focused on patient groups enrolled in trials (Featherstone and Donovan 2002, 2003; Corrigan 2003). While some studies have included aspects of healthy volunteering in their research, which is encouraging, healthy volunteer involvement has often been conflated with patient participation in clinical trials. Problematically, this suggests that the needs and concerns of the two groups are the same, or even that ethical considerations are the same, when in fact they are different.

The research in these chapters is the first sociological analysis of healthy volunteer experiences in the UK and the first to juxtapose professional and lay views, experiences and conceptions of risk in FIHCTs. With increasing numbers of clinical trials taking place every year, and growing demand for human subjects (Petryna 2009), healthy volunteering has become common among sections of the British population. Human involvement in clinical trials has become part of what Schutz (1970:139) has called the social "world of routine activities". Healthy volunteering has become embedded in daily life to the point of becoming normalised. Understanding healthy volunteering in this way helps to bring to the fore the hidden social, political and commercial contexts in which people engage with risk and the problems brought about by medical technological innovations and the "increasing commodification of the body" (Abadie 2010:17).

This is not to suggest that clinical trials and pharmaceuticals have not been explored by social scientists. There has been increasing attention given to these matters by anthropologists who have studied the increased offshoring of later-phase clinical trials and the expansion of the pharmaceutical industry in emerging economies (Petryna 2009; Rajan 2006). Sociologists have also explored pharmaceuticals and clinical trials, including the role of informed consent in clinical trials (Corrigan 2003; Featherstone and Donovan 2003; Donovan and Featherstone 2002; Featherstone 2003; Morris and Bàlmer 2006), while others have analysed the regulation of the pharmaceutical industry within the EU (Abraham and

Reed 2001; Abraham and Reed 2000; Faulkner 2012). Still others have considered the relationship between research practice and the commercial value of clinical trials (Will 2011; Moreira 2011) while Faulkner (2011) has examined prostate cancer screening research and how society has responded to public health campaigns. Hedgecoe (2012) has researched the role of research ethics committees (RECs) – how they are constituted, how they operate and their role in regulating clinical trials. Hedgecoe and Tutton (2013) have analysed sociological and ethical questions that arise out of the use of bodily material in genetic research. Tutton, individually and with others, has looked at the intersection of race and genetics in genetic research (Tutton 2007; Tutton et al. 2008; Tutton 2009).

Studies closest to this research by anthropologists Abadie (2010) and Elliott (2008) and sociologist Fisher (2009) in the US have explored emerging professional subjectivity in human involvement in clinical trials. Abadie's work involved an ethnographic study of a group of anarchists in Philadelphia, living with them in hostels to understand their perception of risk and motivation for involvement in clinical trials. Among his key findings were that the group had become "professional guinea pigs" – people who had made participation in clinical trials a career. Abadie did not define what "professional" meant in this context, whether the group had adopted a code of conduct or whether the term was used loosely to describe habitual behaviour. However, his work provides interesting insights into the lives of some of the people who take part in clinical trials in the US. Similarly, Elliott's (2008) qualitative interview research draws on accounts of healthy volunteers for whom involvement in clinical trials has become a "job". Elliott explores how clinical trials involve vulnerable groups such as homeless people and undocumented migrants to the US. Fisher (2009), on the other hand, looks at clinical trials that involve both patients and healthy subjects; her work illustrates the commercial nature of clinical trials in the US, particularly the interaction of medical professionals, pharmaceutical companies and CROs. She describes how involvement in clinical trials has become a source of healthcare for Americans without health insurance, offering free access to doctors. Though this is not the case in the UK, the possible interaction of healthy volunteering and access

to healthcare is explored as part of this research. Thus, examining healthy volunteer experiences and perceptions of FIHCTs and juxtaposing them with professional views and concepts of healthy volunteers in early phase clinical trials allows this thesis to contribute to the ongoing sociological debates about clinical research and pharmaceutical regulation. Furthermore, this research has the potential to inform policy on issues related to rewards and improving protection of healthy volunteers in clinical trials.

1.6 Structure of the thesis

Chapter 2 reviews the literature and starts by discussing how sociology has studied rationality in recent years by examining research that has explored public views and responses to public health issues such as vaccination. It also examines the central role of bioethics in informing and legitimising clinical trial processes and how it has been influenced by economic and rational conceptions of the individual. The chapter also surveys the different conceptions of healthy volunteering and relates them to the wider debates about policies and guidelines of human involvement in clinical trials. Here I outline the wider discourses shaping concepts of human involvement in clinical trials and regulation in the UK. Among the most influential ideas concerning healthy volunteering are the bioethical principles of autonomy and informed consent. I argue that the discourse of autonomy and consent overemphasises capability and neglects the relationship between social-structural factors – such as poverty, debt and unemployment – as circumstances that may result in people volunteering to take part in clinical trials. Moreover, the commodification of the body in pharmaceutical trials means that inevitably bodies have become "goods" that can be exchanged, albeit temporarily, for the rewards on offer for participation. This chapter also discusses factors such as trust, ideas concerning the "gift relationship" and biological citizenship, all central to the clinical trial process that shapes people's concepts of risks and their actual experiences in clinical trials. I show that in order to develop a better understanding of human involvement in clinical trials, analysis of individual experiences and of the relationship between the individual and the

structural contexts in which decisions to engage with risk take place is required. Chapter 2 concludes by outlining the theoretical framework underpinning this research, namely Schutz's (1970) system of relevance and institutional theory.

In Chapter 3 I make a case for my methodological choices. Taking a phenomenological approach, I was able to able to explore human involvement in clinical trials, including – as participants in this research – regulatory officials, corporate professionals (employees of CROs) and healthy volunteers. I set out on this research very aware of the sensitivity of the subject and the questions I was asking. I was able to account for how this influenced the data collected and the number of participants recruited. This chapter includes a discussion of research ethics and accounts of the challenges I faced when doing research involving corporate professionals on the one hand, and, on the other, the negotiating of access to individual healthy volunteers as research participants.

The regulation of clinical trials has become an important aspect of the drug development process. However, regulation often involves balancing the need for economic development and supporting industry demands with the need to meet public expectations of safer and more effective medicines (Bartfai and Lees 2006). Chapter 4 discusses the regulation of clinical trials by drawing on data from documentary analysis to reveal the structure and organisation of clinical trials. I question the implementation of certain guidelines and explore why some seemingly obvious loopholes in the regulatory system have not been closed. The chapter illustrates how the tensions between political and commercial demands can result in concerns central to healthy volunteer safety being all too easily ignored.

Chapter 5 explores the demographics of healthy volunteers and their motivation for involvement in clinical trials. It employs statistical and interview data to show how, while money might be seen as the prime motivation for healthy volunteering, the relationship between money and the social situations from which participants emerge is a complex one. The chapter also examines the demographics of healthy volunteers, focusing on

factors such as employment, educational attainment and age. It combines statistical and qualitative data to show that healthy volunteers come from varied backgrounds and should not be seen as a homogenous group.

In Chapter 6, healthy volunteering is examined as an economic exchange. Interview data illustrate the tensions volunteers face in exchanging their bodies for monetary rewards. I discuss the ways in which depersonalisation and institutionalisation interact and shape healthy volunteer involvement in clinical trials. Several participants in this study expressed concern at how they are often treated as mere numbers and how they try to retain control and be responsible for their bodies while subjecting themselves to the rules of the CROs during the clinic trials.

The interaction of trust and uncertainty is discussed in Chapter 7. Here I consider ways in which participants in FIHCTs draw on established relationships and perceptions in negotiating risk in clinical trials and what factors influence their degree of trust of pharmaceutical companies. The chapter also illustrates how institutions and professionals view healthy volunteers and how trust and distrust co-exist among volunteers and professionals alike.

The eighth and final chapter encapsulates the main findings of this research. It theorises human involvement in clinical trials by reflecting on the previous seven chapters and in particular how Schutz's (1970) concept of a system of relevances can be used in understanding human involvement in clinical trials. This builds on the issues raised in previous chapters, such as Chapter 4, which analyses the institutional mechanisms in place to regulate the practice of clinical trials. Chapter 8 opens with a summary of key issues discussed in the preceding chapters and goes on to discuss how Schutz's concept of a system of relevances aids our understanding of the complexity of healthy volunteering and the regulation of clinical trials. Through reading Schutz's theory this way, agency is restored to healthy volunteers in clinical trials while still appreciating the ways in which structural constraints influence healthy volunteering. This understanding of healthy volunteering offers a nuanced conception of healthy volunteers not as people who participate in clinical trials

indiscriminately but as individuals who, in attempting to make a living, continuously negotiate and contend with risks and institutional and social constraints. Having outlined the advantages of these approaches, the chapter discusses the limitations and strengths of the research. Finally, it outlines recommendations for policy makers, practitioners and researchers.

Chapter 2
Literature Review and Theoretical Framework

2.0 Introduction: "volunteering" versus healthy volunteering

While human involvement in medical and pharmaceutical research is a long-standing practice, the way in which humans are involved in research today is a new phenomenon. There has been much sociological research on patient involvement in medical research. However, literature considering healthy volunteering in sociology has emerged only in the recent past.

In the previous chapter I looked at how the term "volunteer" is used in discussions about human involvement in clinical trials, whether as patients or healthy subjects. Within the army in the 20th century, volunteering became synonymous with being "committed"; today it is associated with willingness, kindness and in some cases moral responsibility.

In this research, I use the term "healthy volunteer", which is widely understood. My choice is not simply a matter of terminology but also a preferred analytical framework referring to what might be termed the "volunteering turn" following the Nuremberg ruling and subsequent legislation. Firstly, the use of the term "healthy volunteer" distinguishes volunteering in clinical trials from other kinds of volunteering by clearly indicating that the research is concerned with human involvement in medical clinical trials. Secondly, when volunteering is associated with kindness and willingness to help others (Bolton 2005; Abadie 2010), it is likely to be considered in a way that is removed from the context of institutional power interactions in which the "volunteering" takes place. Hence, the aim here is to consider healthy volunteering by studying and analysing the human subjects, institutions and social circumstances (such as debt, unemployment and homelessness) that are often taken for granted, as factors that shape and influence decisions, experiences and perceptions of

risk and subsequent volunteering. Healthy volunteering and the institutions in which it operates need to be brought together in an analytical dialogue because they are imbued with meaning and power and because they influence each other.

There is a need to consider ways in which institutions such as regulators, corporations, political and legislative bodies view healthy volunteers and shape their involvement in clinical trials. This context has been investigated by sociologists and anthropologists in the US. For instance, Epstein's (2008) sociological study on inclusion and politics of science and Fisher's (2009) sociological study on the economy of clinical trials in science and technology studies explored human involvement in such trials, looking at how both patients and healthy volunteers "volunteer" in clinical trials in order to access healthcare. Further afield, Petryna's (2009) research offers an anthropological account of clinical trials in Eastern Europe and Brazil among low-income populations, and of how these trials are linked to healthcare access. Rajan (2006), working on bio-capital in the anthropology of science and technology, illustrates the differences in clinical trial conceptions and practices in India. All these studies, spanning diverse contexts, highlight how institutions influence the conduct of clinical trials. Further analysis of these studies elicits important information about demographic profiles of likely participants in medical research, as well as participants' motivations, backgrounds and experiences. The limitation of such studies is that they have all been conducted in the US, which is different socially and politically from the UK. In conducting this study in the UK the aim was to provide an understanding of human involvement in clinical trials in the national context.

Focusing on healthy volunteers also reveals the ambiguities of the institutional, social and political contexts of low income, debt, and employment in which human involvement in clinical trials takes place. A healthy volunteer may be a willing participant but his or her motivation may be largely financial; it should be noted however that in some contexts, for instance in the US, people take part in clinical trials as a means of accessing healthcare (Fisher 2007; 2009; Abade 2010). The healthy

volunteer is actively involved in negotiating structures and institutional relations, rules and influences that society may uncritically accept. Therefore healthy volunteers should be seen not just as human subjects but as individuals who might well be in debt, unemployed and/or homeless (Abadie 2010) and embedded in a social locale with particular standards and expectations (Johnston and Longhurst 2009). My exploration frames the healthy volunteer as a subject in both social and institutional contexts because different political and institutional contexts may give participants different experiences. Petryna's (2005) work points to such variations in what she calls "ethical variability" (p. 184) and she argues that international codes of ethics governing human involvement in clinical trials fail to take into account the local contexts and lived experiences and how these might shape people's experiences in clinical trials.

This chapter introduces theories that have shaped discussions on human involvement in clinical research and their relevance to this research. Section 2.1 outlines sociological attempts at exploring rationality in everyday life and approaches to risk. Section 2.2 is a discussion of the principles of bioethics, payments to healthy volunteers and the role of trust in dealing with uncertainty in clinical trials. Section 2.3 considers the exchanges, such as bodies for money, in clinical trials in relation to economic and gift relationships. Section 2.4 discusses healthy volunteering in terms of social and moral expectations and "biological citizenship" in which conceptions of citizenship go beyond civil rights to cover the biological constitution of more or less healthy subjects (Rose and Novas 2004). Then follows a discussion of the development of the theoretical framework that will frame my analysis and interpretation of findings: this is the phenomenological approach using Schutz's (1970) concept of system of relevances jointly with institutional theory.

2.1 Sociology and rationality

The idea of rationality in relation to everyday social life has been of interest in sociology from the times of its earliest proponents. In the 19th and early 20th centuries, Marx and Weber both looked at questions about motivation and rationality. For Marx motivation was seen to be the result of material concerns linked to the need to survive, which became problematic as capitalism brought about conflicts between workers and those owning the means of production. Weber's approach focused on explanations for actions. Over time, this work has come to be interpreted as a focus on the verbal justifications or accounts given as reasons for their questioned conduct (Campbell 1996). The approach developed from what Campbell (1996) calls the uncritical reading of Wright-Mills's (1940:907) definition of motive as "anticipated situational consequences of questioned conduct". This definition resulted in the rise of what came to be known as the "vocabulary of motives tradition of inquiry" within sociology (Campbell 1996:101), in which Wright Mills's definition was taken to refer to ways in which motives are presented as explanations in defence of questioned conduct. But as Campbell (1996) argues, this view is contrary to both Weber's and Wright Mills's original understanding of motive as a concept. For Wright Mills (1940), motives should not be seen as mere expressions of intentions and separate from actions; rather, the verbalisation of motive is itself an act just as much as the actions or behaviours in question are. Therefore, analysis of motive should consider more than just the words used in the assumption but should also include the context in which the account is given as well as where the act in question takes place.

It is not surprising therefore, that rationality and motivation have been subjects of interest in much sociological research, precisely focused on explanations for individuals action, in relation to issues ranging from motivations to the kinds of reasoning used by lay people when engaging with science and medicine. Lay reasoning has been well documented in recent research such as a study on health-seeking behaviours in smoking cessation programmes (Bond et al. 2012) and immunisation. In all these

sociological studies, the focus has been on finding logic in lay reasoning. For example, Rogers and Pilgrim's study of public resistance to mass childhood immunisation considered ways in which the public construct their own risk assessments (Rogers and Pilgrim 1995). A study by Hobson-West explored the logic of public resistance against vaccinations in the UK and the implications of this resistance for public health. Hobson-West argues that rather than seeing public resistance to vaccinations as a misconception of risks, or that public decisions on risk are based on comparisons of individual risk, such conceptions of risk and resistance should instead be seen simply as a different ways of comprehending health and disease as categories (Hobson-West 2003). A similar anthropological study by Poltorak et al. (2004) considers the contexts in which resistance to Measles, Mumps and Rubella (MMR) vaccination takes place. Their research questions the focus on parental choice in seeking to explain resistance to immunisation and draws attention to the wider social and personal issues that shape parents' views on immunisation (Poltorak, Leach and Fairhead 2004). A similar study by Mishra and Graham looks at attempts to prevent cervical cancer by the use of vaccination against human papilloma virus. The study focused on the representation of young women as autonomous rational actors in a campaign to reduce cervical cancer in Canada (Mishra and Graham 2012).

Approaches to risk

Closely linked to studies on rationality has been the focus on lay or public understandings of risk. Risk is a highly contested concept within social science. For centuries, society has attempted to define measure, identify and predict risk. However, as a concept within social science risk has become more topical in the recent past (Beck 1992; Furedi 2002). Risk as a concept is to do with the probability of events happening and their potential effects in terms of losses or gains, mostly as a result of some activity or policy (Moldrup and Morgall 2001; Taylor-Gooby and Zinn 2006). There have been several sociological attempts to theorise risk, and today debates about what constitutes risk have become symptomatic of what Giddens (2004) and Beck (1992) call "risk society". However, others

such as Green (2009) have challenged the usefulness of risk as a concept in sociological analysis of health issues. While this debate is important, it is beyond the scope of this thesis. However, knowledge of the value of risk in this sociological literature informed my analysis and was useful in conceptualising my "lay" participants' understanding and decision making about the riskiness of their activities.

However, for the purposes of this research it is important to discuss how risk has been theorised in sociology. According to Beck and Giddens, risks in "risk society" are the result of the artefacts of modern technological innovations; they argue that the social production of wealth simultaneously results in the social production of risks. The limitations of Beck's thesis have been discussed at length in much sociological literature by, among others, Peterson (1990), Tullock and Lupton (2003). Of particular significance to this research are observations by Lash (1993), who argues that the way people view risks (and I add those associated with clinical trials) may be associated with the ways in which they respond emotively and aesthetically by virtue of their socio-cultural and socio-economic context, in this case people on low incomes or those with debts. Medical research professionals may have their views of the same risks reshaped by virtue of belonging to these subgroups and of their circumstances (Lash 1993; Lupton 1999; Mandeville 2006). Furthermore, Lash (1993) states that to understand social responses to risks there is need to consider the role of implicit assumptions, moral and cultural values and practices, and how socio-economic contexts shape perceptions of risk (Enticott 2003). People's willingness to engage in overtly risky activities provides an interesting puzzle for social scientific conceptions of individuals as reflexive actors who intently seek to avoid risks but maximise profits. One view is that this gives empirical evidence for Giddens's conceptualisation of individuals as rational actors always engaging in a risk benefit analysis by consciously balancing potential harms and gains. This representation of the individual tallies with the bioethical conception of personhood that emphasises informed consent in protecting volunteers' interests in medical research (Corrigan 2003). It is discussed in the next section. However, suffice it to say here that Giddens's conception

of the self as stated earlier overemphasises the rational and calculative individual also common among psychologists and ethicists, as capable of controlling their circumstances – in other words as an un-embodied. This view of the individual negates, as Lash (1993) observes, the aesthetic or emotional-expression of a modern self, who is situated in a certain context where both individual and collective practical reasoning, and traditions contour perceptions and responses to risk.

Risk as a concept in this research is therefore used as discussed in sociological literature as mediated or defined by institutions and from a lay individual's perspective. In regards to expert and institutional conceptions of risk, sociologists (Wynne 1996; Brown and Calnan 2010; Otway and Thomas 2006; Otway and Wynne 1982; Fiorino 1990) have explored and critiqued common institutional conceptions of risk in technical and analytical terms. This institutional conception of risk tends to situate risk as purely a technical issue amenable to expert measurement and ranking using statistical models and thus can be mitigated against (Fiorino 1990). Within this context, risk decisions are often thought to be the domain of the experts; experts then mediate and define risk for the public. In this research this is linked to the institutional approaches to managing risks and uncertainty associated with adverse drug reactions in the drug development process (Brown 2010). It is also looked at in terms of the roles played by the MHRA's clinical trials assessment and licensing team who evaluate the safety of the chemical compounds in IMP formulations to ascertain drug safety and RECs. Broadly speaking, within this framework, the experts' role is to assess, define and mitigate against risk, and while lay individuals are seen as rational, they are capable of making informed decision if provided with information by the experts. Hillman (1993) alone and with others, has explored how institutional conceptions of riskiness of cycling in inner city roads influences public perceptions of the risks associated with cycling. They argue that the mistaken view that cycling is more risky than travel by car has led to fewer people taking to cycling due to the perceived risk of accidents associated with cycling. Hillman argues that this view tends to negate how the so-called safe modes of transport, such as car travel, are equally risky and prone to accidents. This is of interest as it

illustrates how institutions and experts play a role in shaping lay views and responses to risk. Horlick-Jones (2004) has looked at emergence of new forms of expertise on risk and how the experts are challenged by the changing characteristics of risks itself. Wynne (1996), Otway and Thomas (1982), and Taylor-Gooby and Zinn (2006) among others in their work have explored differences between institutional and lay conceptions of risk. This difference in views means that lay responses to risks are at times at odds with expert advice and prescriptions. Walls et al. (2004) explored how presence or lack of what he calls "critical trust" in the relationship between the lay public and institutions that define and mediate risk, influences public responses and actions to risk. Brown and Calnan (2010) have looked at the role of trust between lay individuals and institutions in understanding lay responses to risk. This is discussed to some detail later in this chapter. Suffice it to say, as Bendelow (2006) argues, an expert definition and communications of risk tends to negate people's lived experiences and how these contour people's understanding and engagement with risk.

There has been extensive research on risk and lay individual action in sociology among others relating to lay understandings of health and of risk. For instance, taking a broad approach, Horlick-Jones's (2005) paper on logics of risk examines how discussion of public or individual rationality and irrationality often assumes a canonical conception of reason. Canonical here could refer to how rational and economic theories' conceptions of individual action as rational and calculative (Scott 2000; Keynes 2006) have become established as explanations for individual action. Horlick-Jones argues that in practice the lay public's everyday engagement with and conception of risk is contingent on the context and thus adopts a more practical reasoning approach rather than a canonical approach (Horlick-Jones 2005). An important case and of relevance to this research, in investigating approaches to health risk is Bloor's (1995) study of HIV and AIDS transmission. In his work, Bloor looks at how gay male prostitutes conceived of risk. The study demonstrates how people's engagement with risk is contingent on the power relationships involved in their interactions. Lupton and Tulloch (2003) and Kemshall (1998), among

others, look at individual concepts and responses to risk in diverse social situations. Peretti-Watel and Moatti (2006) and Peretti-Watel et al. (2007) have explored conceptions of risky behaviours in health promotion settings. Their findings suggest that labelling people who engage in "risky" behaviours as delinquents brings about pressure to conform to social norms. This, they argue, may make people deny the "risky" label or even the fact that their actions are actually "risky", resulting in an escalation or continuation of the "risky" behaviour. Keeping with the same theme of health promotion, Bendelow, France and Williams (1996) explored how young people view interactions of lifestyle, risk and health. Their study found that for young people engaging with risk was often shaped by the social context, of age, gender, race and class and that health was often not the highest priority on their list of concerns. Of interest in the findings of both Bendelow France and Williams (1996) and Peretti-watel et al. (2007) is how for individuals, accounts of risk seem to suggest how repeated engagement with risk resulted in individuals conceiving of risk as diminishing and in some cases as absent.

Bearing in mind the above discussion, in this research I approach risk by building on Lyng's (2005) conceptualisation of risk and edgework to inform my discussion and analysis, to consider how "consequences of political, economic and scientific progress" and their impact on "health and wellbeing" (Lyng 2009:107) have resulted in public willingness to engage with risk and the emergence of positive views of risk-taking behaviours. According to Lyng, this has stemmed from wide-ranging "neoliberal" policy and political initiatives, specifically in Western societies, which have shifted responsibility for everyday concerns such as health and employment from the state and the wider society to the individual (neoliberalism is discussed in detail later in this chapter). In drawing on Lyng's conception of risk, I am focusing on healthy volunteering in clinical trials not as a leisure activity but as a form of "voluntary" risk taking in which "choice" to engage with risk is delineated, as in high-risk sports (Lyng 2009), by class, race, cultural, socio-economic and socio-political factors.

The studies discussed in this section all have a common theme: understanding individual rationality. Most emphasise the significance of context in understanding risk. In general, society and professionals recognise that that people grapple with issues around risk in clinical trials and that these are often thought to be resolved by the application of procedures informed by bioethics. The following section discusses bioethics and its responses to risks in clinical trials.

2.2 Bioethics and the logic of human involvement in clinical trials

As stated in the introduction, my research is situated at the intersection between healthy volunteering and institutional contexts. In this section I discuss bioethics in order to illustrate its role in this relationship. While the sociological research discussed above focuses on the rationality of the lay public in relation to risk, the application of the canonical conceptions of rationality has not been limited to economics and psychology (Horlick-Jones 2005). Rather, the influence of established conceptions of individual action can also be seen in disciplines such as bioethics. Discussions regarding human involvement in medical research have usually been considered to be the domain of medical ethics or bioethics (Evans 2000).

Bioethics is distinguished from medical ethics in that it is seen broadly to be concerned with attending to a variety of new developments in biological sciences. These include ethical concerns emanating from experiments and human involvement in clinical trials. Medical ethics, on the other hand, is an older discipline dealing with ethical concerns arising from the practice of medicine (Reich 1994; Bosk 1999; Hedgecoe 2004). In this section I focus my discussion on bioethics and specifically on the principlist approach (Evans 2000) that guides the practice of medical and pharmaceutical research. With the banning of forceful use of human subjects in medical research following the landmark Nuremberg ruling (Scocozza 1989; Hazelgrove 2002) came the guidelines and emphasis on voluntary involvement in clinical trials. The aim here is not to give a historical account of the Nuremberg ruling, bioethics and informed

consent as they relate to clinical trials, or to imply that this was the only important event in the history of ethics and medical experimentation. There have been many incidents over the years pertaining to clinical trials illustrated by the Tuskegee (Harris et al. 1996) and thalidomide disasters (Hazelgrove 2005) as outlined in Chapter 1. I raise the Nuremberg trial because it made incidents in medical research visible, and it is also a useful reference point for tracing how discussions of approaches, guidelines and attitudes about human involvement started to change.

Since its inception, the Nuremberg Code has undergone several revisions and has evolved into fundamental guiding principles for human involvement in clinical trials internationally. The involvement of the WHO in promoting these principles and the signing by many countries of these international codes of practice of medical research are indications of how bioethics has become part of clinical trial organisation and regulation and is now woven into codes of practice at national and institutional levels in many countries, including the UK. These principles have been influential in shaping views and debates about human involvement in medical research (Dingwall 2008). Today debates about safety, informed consent and payment of volunteers are all imbued with this traditional bioethical discourse, including a commitment to avoid harming participants and, in a larger sense, achieving good (Evans 2000). Thus bioethics has become institutionalised in the regulatory system as a tool for regulating and legitimising clinical trials and the hub on which the moral practice of medical research is based. This discussion focuses on the dominant principles-based approach of bioethics, which I call "institutionalised ethics". By "institutionalisation" I refer to ways in which ethics and bioethics in particular have become embedded in the organisation, regulation and standards of medical research on which both individuals and organisations in medical research have to model their decisions and practices (Evans 2000; Dingwall 2008). For Evans (2000) the principles of bioethics have such a hold on society that they have become established and linked to ideas of formal rationality. Here differences should be noted between bioethics as practice and bioethics as a discipline. As a discipline, bioethics is concerned with other principles, such as avoiding harm and

duty of care in addition to autonomy and informed consent. These other principles are equally relevant in that they relate to questions about the boundaries between care and medical research in patient involvement in clinical trials (Will 2011), which may easily become blurred as medical professionals assume the roles of both researcher and health professional. In this chapter I consider two principles of bioethics – informed consent and autonomy – and discuss the role of trust in sustaining the principles.

Informed consent

One of the major tenets of biomedical ethics is informed consent. This principle assumes that to protect participants' interests in medical or any other research they should be offered full information (Scocoza 1989; Hoeyer 2009) upon which to base their decision to take part. Within this framework, the provision of full information is considered to resolve most ethical issues as it assumes that it enables participants to make decisions freely and rationally about their involvement. Informed consent is thus seen as a counter to tyrannical and paternalistic medical research practices (Weindling 2001; Corrigan 2003; Dingwall 2008). This model of the autonomous individual is consistent with Giddens's (2004) conceptualisation of the self as rational, free-acting and calculative, and is attractive to governmental regulatory cultures. It can be considered to be an offspring of the increasing importance attached to individualism in Western neoliberal society, with its focus on the autonomous individual and his or her rights.

Autonomy is taken to mean the ability to act freely without restriction or coercion (Beauchamp and Childress 2001; Pescosolido, 1992). With regard to clinical trials, it is often assumed that people take part out of a rational informed choice. The principle is also invoked when addressing debt as a social problem and solving chronic over-borrowing (Walker et al. 2012; Watson 2003). However, using autonomy in such a way negates the social circumstances and the wider social and political discourses in which "informed" decisions are made (Corrigan 2003). This is because the process of consent takes place within contexts of power and against a background of cultural norms that shape the way freedom and

choice are experienced by individuals. In addition, the interaction in which informed consent is given "involves continual negotiation of power that is contingent upon the context" (Lupton 2000:105) in which the interaction takes place. But one may also draw from Milgram's experiments on how people in authority or professional positions may influence people's reactions to risk or obedience to requests, thus compromising the informed consent process (Milgram 1974, Cassell 2005). This further illustrates how power imbalances in relationships may affect what people take on trust or accept. Thus people are likely to be less critical and more ready to believe doctors or other medical personnel, who may be seen as rational and altruistic and held in high esteem.

Voluntarism – the "volunteering turn"

At the core of institutional bioethics is the view that anyone involved in clinical trials or medical research should not be coerced into taking part. This stemmed from the landmark ruling of the Nuremberg trials and subsequent ethical developments such as the Helsinki Declaration, which banned coercion and encouraged voluntary involvement in medical research. In this scenario – what I call the "volunteering turn" – human subjects are expected to consent willingly, coming forward on their own account to be research subjects instead of being forced or deceived into taking part. This development, among others, came about in response to the evidence of abuse suffered by many people at the hands of researchers (Rosner 1996). The aim of introducing voluntarism at the Nuremberg ruling was to restore agency and protect human dignity in medical research.

Chapter 1 gives an historical account on the introduction of voluntarism in clinical trials in response to the Nuremberg ruling. Policy responses to implementing voluntarism in the US and UK did not take place until the 1970s and 1980s. There has been little sociological interest in the UK regarding clinical trials, particularly those involving healthy individuals. However, in the US sociologists and anthropologists have researched human involvement in clinical trials in different ways and at

different times, looking at the relationship between politics, discrimination, the commercial nature of clinical trials and healthy volunteering. Chapter 1 also discussed how the historical analysis by Hazelgrove (2002) and the sociological work of Epstein (2008) demonstrate ways in which the guidelines for voluntary recruitment of participants in clinical trials following the Nuremberg Code were largely ignored in the UK and the US. While Hazelgrove (2002) has also analysed incidents such as the thalidomide scandal in the 1950s and 1960s in which the anti-nausea drug was licensed and sold to the public despite its threat to public health, Bolton (2005) explores how the use of soldiers and other army service personnel was a common practice at the time. Similarly, the works of Epstein (2008) and Washington (2006) on the post-Nuremberg history of clinical trials in the US show how "captive" populations such as prisoners continued to be used well into the 1980s (Epstein 2008a; Epstein 2004; Washington 2006). This was clearly demonstrated in the Tuskegee syphilis study in which black men were recruited as subjects without their consent between 1931 and 1972 (Armstrong et al. 1999; Y. Harris et al. 1996).

The supposedly "strict" application of the Nuremberg Code following the incidents highlighted above in the UK in the 1970s (Bolton 2005; Abadie 2010) meant coercive use of humans in medical research was banned, resulting in the "volunteering turn" in which it was hoped that human subjects would come forward of their own accord to be research subjects. It must be emphasised here that "coercion" refers to making people participate forcefully in clinical trials as research subjects; hence the notion of volunteering became central to bioethical considerations for human involvement in medical research. However, it also draws on economic conceptions of individuals in which people are seen as freely acting and rational (Weber 2009; Scott 2000). To volunteer, therefore, meant people could choose to take part in clinical trials without any force or coercion. In 1964 the Helsinki Declaration revised the Nuremberg Code by drawing attention specifically to vulnerable people such as patients, children and those seen as mentally incapable of making their own decisions; these groups would require special protection in law. People

who do not fit these criteria were (and are still) assumed capable of making rational decisions and representing their own interests.

This shift to voluntarism in the 1970s destabilised what were then established sources of human subjects for research – prisoners, slaves and service personnel (Abadie 2010; Bolton 2005). However, it is argued that forceful and deceitful use of prisoners for research in the UK has never been a problem historically. Whether or not this is true is a matter open to debate. Suffice it to say that these groups were now no longer readily available for use in medical research. As the business of clinical trials coupled with privatisation grew and changes took place in the roles played by pharmaceutical companies and hospitals regarding the conduct of clinical trials in the late 1970s and early 1980s, human research subjects became a scarce resource. Consequently, researchers had to start thinking of new ways of recruiting participants while adhering to the new legislation and requirements regarding recruitment of "volunteer" human subjects. It was during this period that payment to volunteers was introduced. For example, by April 1984 there was such a strong commercial interest in setting up clinical trial units that the government commissioned a working party to look into issues such as the licensing of clinical trial units, volunteer health and safety and the impact of payments to volunteers for medical research. The measure came in response to requests by the Medicines Commission, which had become concerned about the increase in clinical trials requiring healthy volunteers both in the private sector and in the NHS (Royal College of Physicians 1986).

However, this meant that regulators focused on a definition of coercion that involved forcefully and deceitfully recruiting people for medical research. They did not consider the more subtle ways in which coercion might work (O'Neill 2003; Moser et al. 2004), particularly the introduction of payments. In other words, it was not considered that paying volunteers could be seen as a kind of coercion for people who needed money.

Payments and voluntarism

Of particular interest to this project is the issue of incentives in phase I clinical trials with regard to healthy volunteering. The emergence of payments for volunteers in clinical trials cannot be traced to a specific time but allusions to the need to pay participants in research can be seen in the 1950s when a government official talked of increasing payments to research participants at Porton Down. Some observers point to such changes in the early 1970s in response to the civil rights and anti-apartheid campaigns of the late 1960s, alongside public disquiet over the thalidomide disaster and the Tuskegee study (Bolton 2005 and Abadie 2010). For instance, Bolton (2005) shows how in the early 1970s the discourse of a leisure and holiday experience being part of the healthy volunteer experience appeared in advertisements and media coverage of health volunteering at CCRU and Porton Down, a centre for chemical and biological research in Wiltshire. During the same period there were shifts in official discourse at Porton Down as officials started to portray participants in their experiments as "volunteers". They were shown in adverts as being relaxed, as though on holiday, amid entertainment facilities such as snooker tables. Yet participants in these experiments were mainly army service personnel – people who were not normally asked for their consent, but who were used to obeying commands from superiors. It seems questionable that their consent was ever sought or given. Bolton also states that during this time the use of service personnel in military research was endemic and so were incidents that demonstrated consistent negligence. Similarly, the Porton Down unit had "experiment" removed from its title in order to divert attention from any taint of negligence and abuse that was starting to appear in the media and in response to public disquiet over thalidomide and other such incidents (Goldby 1971; Hazelgrove 2002; Bolton 2005).

As human subjects became a scarce and valuable resource, monetary rewards were introduced as part of the commercialisation and privatisation of medical research. The growth in commercial clinical trial

units resulted in a market-oriented approach; healthy volunteers became commodities who could be "bought" on the market. Human subjects in medical research came to be viewed as "volunteers" and capable of rational consent, meaning that from the 1970s onwards, healthy volunteers in particular started to be seen as capable of pursuing and protecting their interests just as though they were making transactions in a market economy. While it must be acknowledged that in deciding whether to take part in clinical trials, subjects are involved in weighing risks against gains, most social scientists (Lemmens and Elliott 1999; Abadie 2010; Petryna 2007; Corrigan 2003) argue that if potential participants are promised large sums as rewards for their involvement, it problematises the entire notion of both informed consent and volunteering itself.

Within this debate, payments are seen as being at odds with the principle of non-coercive involvement as they raise the possibility of participants being exploited because it is thought that most of these volunteers are from economically disadvantaged backgrounds (Schonfeld et al. 2007; Abadie 2010; Geissler 2011; Graduate Fog 2014). This has been found to be true in a variety of recent studies (Corrigan 2003 Rajan 2006; Fisher 2007; Petryna 2007: Abadie 2010). All these studies highlight ways in which structural inequalities – among lay volunteers and professionals and citizens of different countries – and payments to research participants in developing countries or across national boundaries undermine the idea of autonomy in consent and raise ethical dilemmas about the potential for coercion (Corrigan 2003; Rajan 2006; Fisher 2007; Geissler 2011).

Today, providing incentives for volunteers has become common practice especially in FIHCTs, but incentives are also common in later-phase studies. Illustrating the complexity of payment to volunteers in clinical trials, Geissler (2011) looks at how volunteers on an HIV and AIDS vaccine clinical trial in Kenya were offered a bar of soap as an incentive and had their transport costs reimbursed. However, most of the volunteers are thought to have walked to the clinics and the transport refund came to more than the daily cost of living, thus being a kind of

payment for participation in the trials. The researchers were aware of the anomaly, yet the official line was that participants were not being paid.

Corrigan's work examines whether participants in clinical trials in the UK understand the informed consent process, while Petryna focuses on how late-phase clinical trials are being increasingly offshored to developing countries in South America, Eastern Europe, Asia and Africa, in search of populations thought to be less medicated than those in the West (and therefore more likely to be interested in "volunteering" because of their need for medication). Petryna also shows how offshoring is often driven by the desire to realise quick profits by doing trials in countries where costs for doing clinical trials are low and regulation is not as strict as in the West. Researchers and even governments in these countries see pharmaceutical studies as sources of research funding and employment. However, most participants in these trials are poor people who cannot afford healthcare. Anthropological studies by Petryna (2009), Glickman et al. (2009) and Rajan (2006), among others, on the global political economy of pharmaceutical research highlight how the increasing commercialisation and outsourcing of clinical trials abroad raise the risk that research will rely unduly – and unjustly – on economically vulnerable populations. These studies tend to challenge Beck's (2002) argument that risks in the "risk society" have been democratised. Schonfeld et al. (2007) argue that the risks in clinical trials are borne disproportionately by vulnerable social groups who volunteer for the reward that is offered. This makes the issue of monetary inducement relevant ethically in the conduct of clinical trials. It draws attention to the subtleties of coercion – that it can also be traced to circumstances such as debt or other financial stresses that blinker people's conception of risk in the face of alluring rewards (Weindling 1996; Weinstein 2001).

The difficulty with an emphasis on rationality is that it does not take into account that people with low incomes and who are in debt and/or unemployed will see the sums offered for participation in clinical trials as life-changing, while for others such sums may offer relatively little inducement. Nor does it account for the ways in which interactions

between professionals and the public are based on interdependencies and reciprocities.

Another observation worth highlighting here is the point raised by bioethicists Lemmens and Elliot (1999) that legislation at both national and international levels has been vague if not silent about how payments should be calculated. This silence is symptomatic of the assumption of capability on the part of healthy volunteers to represent their own interests and make rational decisions.

The preceding discussion makes it clear that ethics are part of the fabric in which clinical trials are designed, regulated and conducted. It also highlights how rational choice theories and their conceptions of individuals as rational actors have been influential in shaping the principles and practice of bioethics. The view of individuals as rational actors is also apparent in the principles and practice of clinical trials today. It must be emphasised that the intention of bioethics was to restore dignity and agency to individuals, but this has had unintended consequences – the blind spots in the interaction between agency, power and inequality and their capacity to shape each other.

Within theories about economic, rational choice and social exchange, motivation is conceived to be a result of people's expressed wants and goals which influence their behaviour or actions. It is here that rational choice becomes linked to the business of human involvement in FIHCTs. As has been shown, bioethics applies the rational choice theory in its classic sense, by emphasising that the capacity for voluntary action is assumed to emanate from people's capability to make informed decisions. Within bioethics, economic and rational choice theories (Scott 2000) provide the basis for the assumption that adequate provision of information is sufficient to answer ethical questions arising from the interaction between volunteers and researchers in clinical trials. It is assumed that information provision is liberating and enables individuals to make "informed" or "rational" decisions or choices (Corrigan 2003; Weindling 2001). While individuals may be making choices within this framework, rational choice approaches negate the complex interplay of the

individual and the wider social and political structures and how these create a milieu in which certain forms of actions are preferable for certain individuals. Neither model accounts for the ways in which power relationships and wider social factors such as employment, income and cost of living, debts and social expectations come together to make people feel they have to take a certain course of action – such as taking part in clinical trials.

Furthermore, the models seem to portray individuals as calculative and focused on financial benefits but this view does not take into account actions that are motivated by social norms such as altruism. To understand people's involvement in clinical trials requires an approach that takes into account all these additional aspects of individual action, without focusing exclusively on issues of risk and reward.

Trust: in uncertain research

Trust is also an important dimension of bioethics and a key value underlying human volunteering in clinical trials. The role of trust in medical research has become central to debates regarding the medicalisation of populations by the practice of medicine, which has resulted in people trusting and depending on medicines and professionals (Fitzpatrick 1997; Clarke 2010). In encounters between healthy volunteers and medical professionals, the mutual dependencies are obviously not the same as those between patients and doctors. For volunteers the dependence may take the form of monetary rewards – which they need – while professionals need the healthy volunteer's body to test their drugs. This interaction requires trust in order for it to be sustained; the need for trust comes from the risky and uncertain nature of the interactions with regard to outcomes or consequences of the decision and choices made. To address the consequences of risk and uncertainty, bioethics adopts the meaning of risk and uncertainty common in economic theory in which risk and uncertainty are connected concepts associated with outcomes and expectations of the future. Within canonical economic theory, risk is seen to be a probability, and adequate provision of information prepares and

equips people to make rational decisions (Alaszewski and Coxon 2009; Alaszewski and Brown 2007).

The idea of humans as rational calculative actors is controversial within both economics and sociology (Beck 1992, Giddens 2004, Douglas 1992), but rather than address the debate, this research is concerned with risk as it relates to what happens in the interaction between rationality and subjectivity. Risk and uncertainty are seen in this study as separate entities in relation to clinical trials, to refer to the probability of undesirable outcomes as shown by Hawkes et al. (2009). In this framework, risk can be used to describe two aspects of uncertainty, namely the potential danger that comes with it and how individuals respond to the danger (Hawkes, Houghton and Rowe 2009). Uncertainty, on the other hand, refers to "worries or concerns that are often the product of the behaviour of other people"; to deal with uncertainty, people adopt strategies that involve the use of readily available resources such as relationships, feelings and intuition, which are central to establishing trust and distrust (Alaszewski and Coxon 2009:201). Trust can be considered an entirely rational action (Coleman 1990) in which people decide to put faith in a system. Or it can be pre-rational, as when one listens to and respects providers of information before making a choice, or a springboard in cases where an individual lacks knowledge. To compensate for this lack of knowledge the individuals place their hope in powerful institutions or individuals in the hope of positive outcomes (Möllering 2006; Zinn 2008). Given the risky and uncertain nature of clinical trials, it is the role of trust in interactions between research participants and medical researchers that is of interest in this discussion.

There is therefore a need to consider the relationship between professionals and lay people in the conduct of clinical trials. Miller and Weijer (2009) argue that the consent process depends largely on building trust between players. They identify two types of encounters – involuntary and voluntary – in which this may be the case. Involuntary encounters involve working with people who are legally defined as vulnerable, such as children and mental health patients. They are considered involuntary

because they are based on a level of incapacity, which requires that consent must be determined by others. Voluntary relationships are those in which someone deemed capable of a rational decision entrusts another person with important personal issues. Such relationships are established on a basis of a presumed willing transfer of power (Miller and Weijer 2009). An example might be the interactions between patients deemed mentally competent and their doctors, or healthy volunteers and researchers in FIHCTs.

Miller and Weijer further distinguish between the two categories by referring to involuntary relationships as "status relationships" (in which trust is not a factor) and voluntary relationships as "trust relationships". The latter are those in which the individual is deemed capable of willingly entrusting another person with power over specific or shared interests. They are also distinguished by the extent of the differences in power and legal and moral responsibilities and the extent to which the actors are aware of and fulfil these responsibilities (O'Neill 2002). However, both relationships are characterised by inequalities in power and dependence, which challenge the assumption that all players in the interaction have equal power to act in their own interests. Miller and Brody (2003; cited in Miller and Weijer 2009) state that the main bioethics principles of autonomy and informed consent assume that different players in the clinical trial process have an equal capability to protect their interests. Yet this is not possible in relationships involving subjects considered to be vulnerable. Even for individuals who are considered capable of making such decisions, particularly in clinical trials, such encounters also involve vulnerability because of the uncertain outcomes. So both encounters are characterised by vulnerable individuals – patients and healthy volunteers – needing to trust those with power to take reasonable steps to avoid harm.

The transfer of power in these interactions is necessitated by risk and uncertainty that may surround the activity associated with the interaction. For instance, the risk of death for a patient undergoing a new surgical procedure requires trust in the medical professional's decision to act in the best interest of the patient. That many people tend to trust what

doctors say (Mechanic 1996; Pringle 2000) is illustrated in bioethical debates (Melo-Martín and Ho 2008; Appelbaum et al. 2008) and social science literature (Lidz and Appelbaum 2002) on how informed consent is obtained from patients in medical research and the benefits and risks are communicated to patients involved in clinical trials. Though the patient-doctor interaction may be different, parallels can be drawn with volunteer involvement in clinical trials. Healthy volunteers can be expected to trust professional explanations of potential side effects and thus take part in a trial on the assumption that the doctors are likely to act in their interest. Trust can also result from familiarity with the individuals and institutions in a given context (Mollering 2006).

Trust in medical research is central since researchers are not certain of the outcomes of their trials. They are trusted nonetheless because they make a strong commitment to protect the patient or subject from serious side effects or to stop the trial when side effects occur. It is through such claims to commitment to protect participants that trust becomes a crucial part of the transactions and power relations are made explicit. However, some perceptions of the informed consent process and of individuals as rational actors are heavily influenced by neoliberal ideologies of individuality in which capability and vulnerability are looked at in medical terms and individuals are seen as free actors. This view does not take into account the contexts in which risks and uncertainty are encountered and how they shape decision-making processes. These observations show that the nature of the relationships in FIHCTs could be modelled on the trust relationship between patients and doctors, in which volunteers entrust the research team with their wellbeing, placing confidence in their status and expertise. Yet this can leave them vulnerable to exploitation. The main characteristic of the trust relationship is the disparity that results from voluntarily trusting someone else with power over one's life and how much these interactions are imbued with uncertainty or risk. Trust and voluntarism therefore become interconnected.

2.3 Market and gift exchanges: the body in clinical trials

This section considers the concept of exchange underlying human involvement in clinical trials. In viewing healthy volunteers as capable of rational consent, an exchange inevitably takes place: the volunteers submit their bodies for trials and in return receive the rewards offered. Medical sociology needs to examine issues of human involvement and social differences and their roles in medical research. The commodification of the body has become topical in social science, in the studies of anthropologists Scheper-Hughes (2000), Sharp (2013), Moore and Schmidt (1999) and Lock (2007). Sociologists such as Wardby and Mitchell (2006) and Cooper (2013) have also explored the topic and how in some cases the use of the body reflects social capital (Bourdieu 1985; Wainwright and Turner 2003). A sociological analysis of how the body is objectified, as an object for research, and commoditised in everyday life is useful in understanding people's perceptions of risk and their motivation to engage with it.

Market exchanges?

In Section 2.2 I discussed how anti-apartheid and civil rights campaigns, scandals such as the thalidomide disaster, and the growth of the pharmaceutical industry in the 1970s, resulted in an emphasis on voluntary human involvement in clinical trials. Human subjects became a scarce and valuable resource. Cooper and Waldby (2014) observe that in post-Fordist political economies there has been a shift from mass production to service economies and knowledge production; flexible working has been introduced, involving contracts in which individuals rather than employers are responsible for the risks at work.

Cooper and Waldby (2014) argue that the response of post-industrial economies to emerging economies has been to focus not on mass production but on biotechnological and ontological innovations that would surpass the achievements of the post-industrialisation era. The accompanying policy discourse has focused on the unrealised potentials of biofuels, genome projects and efforts to harness them for the growth of

their economies. Yet there has been little research into how these bio-economic ideas move from ideas in the laboratory to experiments on human beings. It is through the process that I call "passive labour" that value is produced. Today the pharmaceutical industry demands increasing numbers of research participants, and the search for volunteers has gone beyond national boundaries (Petryna 2009; Rajan 2006). The growth in CROs and the global scramble for healthy subjects for clinical trials is an illustration of the value that human subjects in research contribute to the bio-economy.

Within medical research today, human involvement may be conceptualised as an economic exchange: healthy individuals are used to test new drugs in exchange for the money offered by research companies (Elliott 2008; Abadie 2010). This exchange can be traced back to mediaeval times. Until recently the poor were used as subjects for such trials because it enabled them to receive healthcare and in some cases test the remedies of their masters (Washington 2006; Weinstein 2001). Today, healthy volunteer participants in research are often from vulnerable populations which do not stand to benefit from the medicines being tested on them. The issue of taking part in clinical trials to access healthcare features in key debates about clinical research in developing countries such as Kenya (Geissler 2011). Though this may not apply in FIHCTs, the notion of the poor as participants contrasts starkly with the demographics of healthy volunteers in the US. This development in human involvement in medical research feeds on the dominant conceptions in which individual choice and consumption are closely tied to the idea of liberty (Higgs 1998).

Anthropologists Lock (2007), Petryna (2005, 2007, 2009) and Rajan (2006) illustrate how recent biotechnological developments have transformed the bodies of human research subjects and all their constituent parts into valuable material. Blood serves as the basis for immortalised cell lines and is an important commodity in pharmaceutical research. Sperm, embryos and other body parts such as kidneys have acquired commercial value both to pharmaceutical companies and to the public, especially financially disadvantaged people (Lock 2007). The

demand for healthy volunteers in medical research has led pharmaceutical companies to search locally and globally for cheap and accessible subjects. Petryna draws attention to how the application of ethics seems to vary across international boundaries, specifically among populations of different economic status; such variability obscures who governs the conduct of clinical trials and who is responsible for protecting the rights of clinical trial participants. Petryna's notion of ethical variability is equally important in this study because it may be applied to an interrogation of regulatory frameworks and the interpretation of ethical guidelines. Moreover, professionals with easy access to bodies realise they possess a capital resource (Harding 2000; Petryna 2009; Cooper and Waldby 2014), despite the risk of harm that their products and trials hold for humans (Lupton 1999; 2000; Flynn 2006). The difficulties of recruitment and efficient running of trials have provided a growing market for CROs, which recruit subjects and carry out research on behalf of big pharmaceutical companies, and there is increasing competition for research subjects.

The nature of the exchange in these trials is also closely tied to technological developments; human bodies and body parts are now used openly in such exchanges as resources for medical research or treatment. Medical technological innovations since the 1950s have increased transfers of body parts in complex operations to save lives or pursue projects like parenthood. While most of these parts can be harvested from cadavers, organs and tissues such as kidneys and bone marrow from living persons are today common candidates for transfer. It is not only institutions that see the body as a resource; individuals, too, see the potential of their bodies to generate income. Actors on both sides of the equation are trying to make the most of this resource. There has recently been a growing supply of surrogate mothers and egg and sperm donations among poor communities in parts of India (Aristarkhova 2005; Roberts and Scheper-Hughes 2011). Healthy volunteering has become routine among some groups. Abadie's work, discussed in Chapter 1, shows how some healthy volunteers have come to see their bodies and body parts as resources with which to make a living. It is here that morality, specifically questions about what is an acceptable way of making a living, and individual agency collide.

Given the commercial prospects of the human body in clinical trials, there has been an increase in debates around the role of the human subjects or their bodies. Of interest here is the fact that while in market exchanges, goods swap hands and ownership, in clinical trials healthy volunteers retain the ownership, "control" and responsibility of the body while sharing or lending their bodies for research. This adds to the complexity of exchanges in clinical trials.

Anthropologists Scheper-Hughes (2000), Sharp (2000) and Grub (1998) raise concerns about viewing the body as a commodity possessed by autonomous individuals. They argue that conceiving of human subjects as a valuable "resource" is symptomatic of consumerist, neoliberal tendencies in which the focus is on free markets, individual liberties and reduced state regulation. By neoliberalism here I refer to aspects of the liberal traditions that stand against government intervention, in the form of restrictions and barriers, in economic matters. In this way, individuals are seen as rational actors capable of participating freely in self-regulating markets. State regulation is reduced to creating an environment that fosters a free market or imposing protectionist policies to favour local industry and commerce. Neoliberal approaches are demonstrated in state policies of privatisation of public services, including aspects of research, and deregulation. Fisher (2009) observes that neoliberalism also entails the state's transfer of its responsibilities to the individual citizen. Part of the rhetoric of individual liberties is that the state should not interfere with individual choices; rather people should be allowed to participate of their own accord in the market thereby providing for themselves. Neoliberalism is prevalent in healthcare in the UK, as seen in the growth of the CRO industry, the emphasis on choice and the emerging debate about marketisation of healthcare in which patients are regarded as consumers (Haynes 2003). Understanding human involvement in clinical trials requires an awareness of how their conduct and regulation are influenced by the neoliberal approach, which extends beyond privatisation to include the commodification of the body. Discussions about healthy volunteers are framed within ideas of liberty and consumption while limiting options for the individual with a discourse of

rationality and efficiency. At an institutional level, healthy volunteers become consumers.

The over-commodification of the body often occurs under the guise of a "gift exchange", free choice and voluntarism, with participants portrayed as individuals interested in helping society or capable of making choices. But as Sharp and Giessler (2011) argue, such an approach masks the suffering and pain endured by many who subject themselves to these trials and obscures the value of the exchanges. Neoliberalism espouses a view of self-regulation by professionals on the one hand and by individuals on the other. Here the focus is on how self-regulation works both at individual and institutional levels in relation to rationality and subjectivity within neoliberal conceptions of the individual and state regulation of clinical trials. Allowing the body to be used in exchange for payment is justified – healthy volunteers are seen as capable, consenting adults who should be allowed to do whatever they wish. Viewing human subjects as rational actors negates the effect of unequal power and disadvantages in the exchange process. There is also the assumption that all players have equal access to resources and influence and thus take part in the market on an equal footing with everyone else (Massey 2013).

Studies of volunteering today allude to the phenomenon that poor populations, especially in developing countries, are tested with drugs, which, once approved, are sold to wealthy populations in the West (Shah 2006). But in the absence of clear demographics it is difficult to ascertain to what extent the poor are over-represented in clinical trials, and specifically in FIHCTs. Bioethicists Lurie, Wolfe and Angell analyse later-phase trials in Asia and sub-Saharan Africa for the prevention of mother-to-child transmission of HIV, in which drugs were tested unethically on humans by researchers keen on obtaining quick results (Lurie and Wolfe 2012; Angell 1997). Anthropologists like Petryna (2009) consider the conduct of trials in Brazil and Eastern Europe on populations that are desperate for adequate healthcare. While the issues that this literature raises are important, most of the focus has been on later-phase trials. There has been no sociological discussion on early phase trials, whether they take

place in poor countries and how they are carried out. There are no clear data showing the demographics of participants. Regarding healthy volunteers, for instance, Abadie's and Fisher's studies cited earlier in this chapter discuss healthy volunteering in the US as becoming almost a profession and how this could be linked to a lack of jobs and permanent employment among some social groups. Nevertheless, both studies depend on data summarised from qualitative research and do not provide adequate demographic details; there are no data that could confirm that the poor are over-represented in clinical trials. Such data would advance the critique of neoliberal framing of healthy volunteering by capable participants with free choice in a free market.

The gift relationship?

The exchange has not always taken the form of economic exchange; volunteering for medical research or medical donations can be construed a "gift" exchange, with underlying altruistic motivations. Within this context, medical research and human involvement in the testing of drugs and health technologies are construed as "a gift". This section draws on Titmuss's (1971) work on the gift relationship associated with blood donations. Titmuss's theory of gift relation is based on a comparison of altruistic blood donations in the UK and paid donations in the US, and the relative success of their systems for gathering blood. His thesis addressed voluntarism and he is credited with making an important contribution to policy – an official task force in the US was commissioned to respond to his observations. Today the concept of the gift relationship is used widely and in many contexts (Robinson et al. 1999; Berridge 1997).

However, the gift relationship has not been without its critics. Among the concerns raised about Titmuss's work is the way in which he portrays a social and biological need to help in an essentialist way. Some question his assumptions about the altruistic capabilities of the average citizen (Page 1996). Others question the applicability of the concept of gift relationship in traditional societies that are responding to changes brought about by modernity (Mauss 2002; Douglas 1999). Moral discourse about human involvement in clinical trials is prevalent in the research literature

today because of the debates about donations of organs and blood and, indeed, healthy volunteering in medical research as a "gift". The Nuffield report of 2011 on donations of human body parts, which was strongly influenced by anthropology, also emphasised the role of the gift relationship in healthy volunteering in clinical trials. Studies on motivations for human involvement in medical research (Hallowell et al. 2010; Fisher and Kalbaugh 2012) show that some patients participate in clinical trials to contribute to the development of life-saving drugs. In this literature, healthy volunteers are described as at least potentially altruistic.

What the discussions do not seem to take into account is how people's responses to questions of motivation, especially in surveys if used for data collection, can be influenced by the need to fit with socially desirable views; if asked in a questionnaire why they chose to volunteer in clinical trials, respondents are likely to tick the box for "altruism". In patient recruitment advertisements, altruism is always given as a major reason for doing clinical trials. As Fisher and Kalbough (2012) observe, in positioning altruism front and centre, professionals teach patients how to respond to questions about their motivations, using altruism to minimise potential conflict between care and research in a caring setting such as a hospital. There is therefore a need to carry out research that explores the assumptions of volunteers beyond their perceptions of an acceptable response to questions about their motivation. There is also a need to explore the context in which this altruism takes place and how it is shaped (Morris and Bàlmer 2006).

Some work has also challenged the universal way in which the gift relationship (TGR) has been applied to human involvement in medical research and the wider context in which "gift" exchanges take place: for instance, Levi-Strauss's work on anthropological economics. Bourdieu's work usefully draws attention to ways in which TGR creates social ties and obligations similar to economic debt, since once given a gift cannot be returned without causing dishonour. In gift exchanges, obligations and rules are often implicit, and debates about gift giving in human involvement in clinical trials do not take into account the expectations or

reciprocal nature of gift exchanges. In every culture exchanges of gifts are governed by rules, some of which may bind people to give something in return; in others, saying "thank you" may not be seen as an adequate expression of thankfulness. It is possible that in other contexts receiving a gift makes people begin to feel obliged to reciprocate the gift or gesture. In doing so, the gift exchange becomes an exchange based on benefit but also fulfilling social norms rather giving freely. For instance, Douglas (1990) and Weiner (1992) point to ways in which the gift exchange creates enduring commitments symptomatic of principal institutions. Within these institutions people are implicitly expected and obliged to reciprocate the gift. Giving gifts assumes different meanings, including one in which it is viewed as an imposition to and collusion between those involved in the exchange with some social meaning attached to the exchange. In this way gift giving does not occur in a vacuum but takes place within a moral space with defined, though often implicit, rules about how people should respond when giving gifts. Any gift giving or acts that break these moral codes are often looked down upon or in some cases can be punishable. Only some objects are seen as gifts, which suggests that the focus should be on the subtleties of human relationships and interactions. For instance, one would question whether all claims of altruism in patients are sincere, which highlights the moral and political nature of human involvement in medical research and the ethical decisions that have to be made. These concern how the limits of personal and, for healthy volunteers, economic interests are to be delineated. The investigative conclusions of the sociological and anthropological literature discussed here indicate a need for an analytical approach that examines "gift giving" and exchanges (in this case volunteering in clinical trials) over time as potentially habitual and repeated actions and not merely focusing on the act of "gift giving", or volunteering in a clinical trial, as a self-contained phenomenon. Also to be considered are the role and influence of power and context in which exchanges take place.

This section has considered how human involvement in clinical trials may take the form of both economic and gift exchange. The chapter overall has reviewed the debates, both academic and ethical, that have arisen as a

result of human involvement in medical research. The main theory underpinning economic and gift exchange models is the economic view of individuals as rational actors and the assumption that healthy volunteering is motivated among some people by economic gains while for others by altruism. The limitations of both these views have been discussed as well. In the following section I develop the idea of morality and consider ways in which human involvement in clinical trials becomes an issue in the much larger context of citizenship.

2.4 Healthy volunteering: moral responsibility and biological citizenship?

The term "moral" is used here to refer to a common social understanding of what is right and wrong, rather than the meanings governed by ethical principles common in academic discourse. I draw on Zigon's (2009) conception of sociality and morals as being distinct from ethics in that morals as used in everyday life can be seen as habitual (Schutz 1970) while ethics involves a "stepping away from this habitus", particularly after one's conduct is brought into question by others, thus prompting an ethical response (Zigon 2009:2).

In this study, questions about morality can be seen in two ways: first, as moral dilemmas about the use of the human body for medical research in relation to socially acceptable ways of using the body to make a living. In this case, moral questions are asked of healthy volunteers who get involved in clinical trials for money. Second, is the question of whether human involvement in clinical trials concerns the responsibilities of all citizens. In this section, I will discuss these two questions and conclude with the implications for human involvement in clinical trials.

Moral responsibility or irresponsibility?

There has been much debate among ethicists and sociologists as to whether it is right or wrong to invite and pay volunteers for participation in clinical trials. In the discussion on economic exchanges and the role of the body, I drew on Scheper-Hughes (2000) and Sharp (2000) to illustrate the moral implications of the use of human subjects in medical research.

The moral implications are not about the choice some people make to take part in clinical trials, but rather about the fact that involvement in medical research for the reward on offer seems to attract people who are financially disadvantaged. In this context, it needs to be asked whether it is degrading to allow humans to subject themselves to such trials in order to make a living. The question draws on socio-cultural stipulations which define acceptable and unacceptable activities in which individuals may be involved (Zigon 2007). Sex work is a related area and is shown to attract stigma and labels of recklessness and carelessness (Cobbina and Oselin 2011; Bradley 2007). Other studies point to ways in which inequality, poverty and intergenerational disadvantage in society results in certain people being driven to sex work and, indeed, healthy volunteering, to make ends meet (Kempadoo 2003; Sanders 2005; Leggett 1999). The risky nature of clinical trials means that volunteers are sometimes seen as desperate and reckless people seeking quick rewards rather than doing a "normal" job, and their rationality and morality, like those of sex workers, are often brought into question. However, healthy volunteering and sex work present an opportunity to question the meaning of "normal" jobs, especially in a neoliberal market economy. This is because in many ways the motivation for engaging with risk can become embedded in cultural practices; over time the moral lens becomes the "normal" lens through which engaging with risk by volunteering in a clinical trial or similar risky work is viewed. This makes it easy to ignore the wider context in which such actions and behaviours take place.

In a way, today's views on healthy volunteering relate to Scott's (1977) idea of moral economy. His work draws attention to the need of poor peasants to produce enough to support their families while meeting the social expectations of their society and the risks they take in order to survive (Edelman 2005; Daston 1995). Scott explored the struggles of peasants during years of famine in Burma and Vietnam in the 1930s when they demanded access to land, the right to glean on farmlands and fair market prices. A parallel can be drawn with the ways in which people are living on the margins in the UK today. Social expectations can influence how people respond to social problems such as unemployment, loss of

jobs or even extreme poverty. Questions about healthy volunteering are therefore taken to be ethical questions about how institutions use human subjects in medical research, asking whether it is right to encourage people to engage with risk by paying them huge sums. But the morality of healthy volunteers is also often questioned by society: why are they so willing to subject their bodies to such risks for the monetary reward offered?

Biological citizenship?

Social scientists Petryna, Rose and Novas also examine the moral aspects of taking part in clinical trials – not only the rights or wrongs about the use of the body in this context but also how the moral obligations of citizenship have come to include what they call "biological citizenship". The meaning of citizenship, they argue, has broadened to include not just civic duties but also issues to do with the biological reality of human beings whether as individuals or as members of communities (Petryna 2004; Rose and Novas 2004; Leach and Scoones 2007). Petryna's anthropological study considers the Chernobyl incident and how it shaped the survivors' experience of citizenship with regard to their claims to biomedical resources and justice. The research also looks at how at-risk populations are created through scientific discourses and institutions. For Rose and Novas, biological citizenship stirs a collective sense of community in terms of support for people's rights to treatment and pooling of information. At the individual level, they merge their knowledge about their biological being, resulting in widespread individual acts of personal responsibility. Others such as Fitzgerald apply the concept of biological citizenship to understanding ways in which the activism of people suffering from rare genetic conditions are organised, how they respond to medical and scientific expertise, and their political goals in negotiating and accessing treatment (Fitzgerald 2008).

Here citizenship is linked to access to healthcare and the responsibility of members of society in ensuring health access. In bioethics the work of Harris has particularly been explicit on what he calls everyone's duty to take part in clinical trials (Harris 2005). This work is linked to views about volunteering in medical research as a "gift", as

discussed in the preceding section. According to this view, volunteering is seen as a social good and of benefit to everyone. So while being involved in clinical trials can mean individuals are stigmatised as reckless, others clearly see it as a noble thing to do. Participation in some trials that are seen as less risky – particularly later-phase studies for patients seeking treatment for long-standing illnesses – are considered particularly noble and socially acceptable. Phrases such as "helping future populations and patients" are common in recruitment advertisements (Abadie 2010). Similarly, biological citizenship as a concept is useful and relevant here as it sits well with conceptions of the body in liberal debates in the "volunteering turn". Volunteering therefore seems to take on the meaning of a moral duty, something done for the betterment of society, an attitude that is seen to be a motivation for taking part in clinical trials (Almeida et al. 2007; Hallowell et al. 2010).

The problem with the view of the body as a national resource with a duty of citizenship is that it overlooks the circumstances in which such acts of citizenship are practised and how people are motivated to take on such a duty. For instance, patients take part in clinical trials because they are looking for a solution to their health problems; healthy volunteers may participate not just for altruistic reasons but also for monetary gain. The benefits of drugs trials are not always enjoyed in the countries where the trials are carried out, but rather in the West. Petryna (2004) Rajan (2006) and Shah (2006) show how people who are poor or unemployed are more likely to be research subjects in trials whose findings do not benefit them. In such instances issues of inequality, marginalisation and nationality are inevitably raised.

Biological citizenship is linked to biology and human worth, and unequal experiences are often brought to light. The different ways in which biological citizenship is experienced are reflected in discussions about the importance of human bodies to science and about citizenship among patient populations, specifically the political representation of certain racial groups (Epstein 2008a). Epstein examines how participation in medical research can become a political issue in the US because of the profits that

are perceived to result from the knowledge created in such studies and benefits to different groups in society. Pollock explores the racialisation of drug development in the US, raising questions about the scientific justifications for targeting racial groups in the drug development (Pollock 2008). Tutton looks at the inclusion of ethnic minority groups in genetic research in the UK (Tutton 2007; Tutton 2009; Tutton and Prainsack 2011)[2]. Biological citizenship should also take into account the influences from within communities and how people conceptualise their identity as citizens. Thus citizenship can create a sense of duty to others, to family relations and the community and be a basis for claims to particular rights and services (Petryna 2004). Biological citizenship therefore becomes "both an individualising and collectivising" tool (Rose and Novas 2004, 5) as individuals begin to see themselves as having to conform to the norms of wider society.

[2] *Though this present research does not focus on issues of race, it is an important aspect of human involvement in clinical trials that is worth exploring in phase I clinical trials as well.*

2.5 Developing the theoretical framework

So far this chapter has discussed some of the theoretical concepts and substantive debates that have shaped my understanding of healthy volunteering. This research focuses on human involvement in clinical trials, precisely FIHCTs involving healthy volunteers. While monetary payment is a motivation for taking part in clinical trials, discussions about why people take part in clinical trials mainly focus on patient groups predominantly portraying volunteers in clinical trials as altruistic or seeking treatment. There has been insufficient interrogation of the contexts and circumstances in which people make decisions to take part in clinical trials. Anthropological literature on global offshoring of clinical trials shows how people in diverse socio-economic and socio-political contexts in the Global South take part in clinical trials. The literature has also critiqued bioethics frameworks especially with reference to therapeutic misconception and justice (Appelbaum et al. 2008; Lidz and Appelbaum 2002). In this context, structural inequalities in access to healthcare and income are said to constrain the choices of populations in the Global South, particularly in poorly organised and underdeveloped healthcare systems in countries such as Brazil and India (Epstein 2004; Petryna 2004; Rajan 2006; Fisher 2007) where people take part in clinical trials to access healthcare. However, it is also important to apply sociological analysis to the wealthy North where involvement in clinical trials is seen to be purely a matter of "choice". It is important to interrogate the context in which people take part in clinical trials and how perceptions of choice and freedom framed within neoliberal terms in the West obscure the socio-economic and socio-political conditions that make healthy volunteering look like a worthwhile option.

In Section 2.1 I looked at how bioethics has become part of the fabric through which clinical trials are designed and take place. I have also discussed the limitations of the bioethics principles of informed consent and voluntarism, further stressing the significance of trust when dealing with risk and uncertainty. Furthermore, the chapter has examined the influence of rational and economic theoretical approaches to risk and concepts of individuals in ethical policy considerations. I have considered

how these approaches view individuals as rational actors capable of giving considered consent. The discussion has highlighted how these approaches have been key to informing our understanding of consent in ethical debates. However, I also illustrated the potential limitations of these theoretical approaches in helping to explain risk and motivation, especially in the context of clinical trials. Essentially, there is a tendency within these frameworks to over-emphasise capability; assuming everyone has equal access to resources while negating structural and institutional impacts on people's motivation to engage with risk. I also considered how these approaches are not useful in explaining behaviours that may be habitual and repetitive in nature (actions that people would normally engage in without much prior thought or calculation). Therefore, to better understand human involvement in clinical trials there is a need to consider the relationship between subjective and institutional contexts in which people engage with risk. Although the idea that people take rational actions has often been widely recognised in sociology and beyond, within sociology and anthropology it is acknowledged that people engage in both rational and non-rational actions in everyday life. Nearly a century ago, the anthropologist Malinowski (1921) considered social exchanges as entrenched in structures of reciprocity and social obligations. Weber (1920) focused sociologically on the typology of action and he considered similar issues (Scott 2000). To understand healthy volunteering and its interactions with institutional mechanisms requires an approach that considers the role of habituation, emotions and other dimensions underlying human action such as value-focused actions lacking rational calculation and how these are also shaped and mediated by institutional influences. A phenomenological approach enables such an analysis to be carried out.

2.6 Phenomenology: motivation, risk perception and social constraints

A phenomenological perspective on social action focuses much attention on actions that are often unconsidered and taken for granted. Such actions are typically seen as routine and involve "the suspension of these unconsidered certitudes and an explicit analytical interest in the

previously implicit" (Bloor 1995:97). Using this approach in analysing human involvement in clinical trials adds to the critique of "decision" and our understanding of how decisions to take part in clinical trials are made. This social arena of unconsidered actions, beliefs and unspoken understandings is what Alfred Schutz (1970:139) refers to as the "world of routine activities" – familiar topics, conversations, habitual expectations and routine behaviour (Bloor 1995). Some motivations for engaging with risk may be calculative, such as volunteering with the purpose of receiving money to pay off debt, but volunteering in clinical trials with other motivations and without any prior calculation also happens routinely and repeatedly, with relatively little reflection. For instance, Abadie (in Section 2.5 above) writes that people who take part in clinical trials as healthy volunteers often do not consider other options available to them. The tension between calculative and routine action is Schutz's main interest. Similar discussions can also be seen in the work of Bourdieu (1990) on attention and habituation.

For Schutz, however, the distinction between familiarisation and thoughtfulness is as a result of the changes in thinking that happen when individuals are repeatedly confronted with similar incentives. When faced with a new situation people may take time to think through the available courses of action. Not all options available will be suitable; some decisions may be delayed until one course is considered appropriate. However, with routine activities the complex cognitive processes fail; an individual has to make a rapid appraisal of the problem and action is taken without much consideration of other options. This illustrates how cognition is both a "polythetic" (step-wise) process and a "monothetic" (single flash) process (Bloor 1995; 97). Polythetic decision making can be seen in theories of behaviour that focus on the cost-benefit analysis (Schutz 1974) of risk taking. Much as this may be helpful in explaining behaviour, it does not take into account the different contexts in which decisions are made. What is needed to understand risk-taking behaviour, therefore, is an exploratory framework encompassing both the new and the routine in the decision-making process of social interactions.

For Schutz this can be achieved by using a "system of relevances", which collates a variety of perceptive activities within one framework. This refers to the ways in which individuals position perceptual stimulations. There are topical, interpretive, motivational and interpretive relevances (Schutz and Luckmann 1974). These are divided into sub-categories depending on whether the stimulus is volitional (intrinsic) or imposed. Each of Schutz's relevances can be extended depending on one's interest in the activity and the extent to which one may be familiar with the stimuli (Schutz 1970; Bloor 1995). Relevances are determined by the biographical situation, which for Schutz refers to ways in which one's views and beliefs, shaped by the social context they are exposed to, provide the source of the stock of knowledge; this socialisation thus shapes individual views, beliefs and responses to social stimuli (Schutz et al. 1974). Topical relevances define whether the circumstances are a problem for the individual and whether interpretation of the issue at hand will be required of the individual. Topical relevance comes into play when something does not fit prior knowledge or expectations and thus the topic or issue becomes relevant to an individual. In other words, topical relevance arises when things become questionable to the individual and this happens for certain specific reasons (Goettlich 2011). Intrinsic topical relevances denote the voluntary quest for interpretation while the imposed stimuli denote the constraints. The extent to which an issue becomes topically relevant depends on previous knowledge, experiences and the degree of uncertainty the situation brings. For instance, a woman who has grown up knowing that using an intradermal implant is the best form of contraception goes to her doctor and requests one. After the assessment, the doctor inserts the implant. Until this stage, the implant as a form of contraception is not topically relevant, according to Schutz's terminology. However, after having the implant, she is asked in a conversation with another friend if she had done some research before deciding on this form of contraception. Had she considered its potential side effects and general safety? At this point the implant becomes topically relevant – she becomes uncertain about the safety of the implant and starts to question her actions; hence the need for interpretation (interpretative relevance).

Interpretative relevances refer to the restricted knowledge the individual may possess regarding the issue at hand (Schutz and Zaner 1970) and to aspects of topical relevance which need an interpretation or further understanding; this is because not every aspect of the subject might need understanding. Similarly, only the interpretive relevance of the stock of knowledge defines what part of the stock of knowledge to use in the interpretation. The individual may draw on previous experience and knowledge to interpret the uncertainty that the encounter brings. Using the example of the implant above, the woman may begin to ask what the implications are if the implant becomes harmful to her health, and what that might mean for her life in general. In seeking to understand the situation, the individual may come to the conclusion that the implant is safe and that there is no need to worry about it. Alternatively, the individual may become more uncertain about the safety and even question her decision to have an implant in the first place. At this stage, the implant becomes motivationally relevant.

Motivational relevance refers to what Weber (1968) refers to as the "adequate grounds" upon which human behaviour is based. Schutz, to an extent, espouses Weber's notion, but sees motives as composed of "in order to" and "because of" motives. "In order to" motives generally refer to "because of" motives after one has taken an action concerned with the future and yet building on past experiences or knowledge (Schutz and Zaner 1970). The process of interpretation and taking steps to deal with the situation is complex and does not follow the order outlined in this section. As mentioned earlier, decisions may sometimes be kept on hold while other options are investigated so that competing or conflicting options can be discarded. On the other hand, the process can be momentary, due to only marginal interest in the matter (which can involve the category of motivational relevances) and as a result of an individual's pre-existing familiarity with the situation. This results in the individual drifting into a monothetic mode of thinking (Bloor 1995). Again, to use the example of the implant, the woman might decide that there is no need to worry as there are many other women who have implants and they are well; or she may simply trust the doctor's explanations about the safety of

the implant. On the other hand, she may have all the available information about safety risks associated with implants but still decide to have the implant because she prefers it to contraceptive pills, or she is convinced that the side effects will not affect her. Alternatively, the woman might reconsider the information regarding risk and ask to have it removed. This illustrates one framework for understanding the decision-making process and how decisions are sometimes based on limited information and without much prior thought.

The system of relevance has been used in sociological research in different contexts. For instance, Bloor's (1995) research on the sociology of HIV transmission used this approach to explore the contexts in which decisions involving risk among gay male prostitutes take place. He found that in most cases decisions are shaped by an interplay of personal factors such as an individual's ability to handle a client, or a tendency to want to avoid conflict with the client. All these aspects were crucial in shaping responses to HIV infection risks in these contexts.

The above discussion illustrates the investigative significance of Schultz's system in the conceptualisation of motivation and risk perception. One of the merits of using the system is that it draws attention to the circumstances in which action takes place instead of the preconceptions the individual brings to the situation. This provides a good basis for exploring volunteering and regulation in clinical trials – not only from an individual perspective but also considering the wider socio-political and economic milieu in which volunteering takes place. The system also highlights the distinctions between polythetic and monothetic decision-making processes, and volitional and imposed dichotomies which are often unaddressed in theoretical explanations of motivations and risk perception. Using Schultz's system of relevances and considering both volitional and imposed dimensions of action enables us to observe how individual circumstances interact with institutional or structural influences in the context of volunteering for clinical trials.

The individual and structural elements of Schutz's system of relevances

One of the criticisms of Schutz's approach is that it is overly subjective in its perspective on human action. However, the theory of the system of relevances does imply structural considerations. As discussed above, Schutz considers both volitional and imposed aspects of motivation underlying human action. It is the imposed aspect that is of interest here as it implies outside influences or pressures. I am particularly interested in uncovering institutional or structural influences on the decision-making process among human volunteers. In this case, I adopt a phenomenological approach to institutional theory to provide the structural analysis for the discussion.

In this research, the notion of institutional forces or pressures refers to forms of social action or rules that have been established over time. These involve both bodies of knowledge and sometimes even actual organisations; in the present research, for example, bioethics as a discipline brings biology, health and ethics together to provide a framework for understanding the moral implications of human participation in clinical trials, while committees, advisory groups and other organisations have emerged to consider the moral and rational dimensions of volunteering. Institutional considerations within phenomenological institutional theory consider the ways in which structures, rules, systems, norms and routines become normative and influential guidelines for social behaviour (DiMaggio and Powell 1991). The focus therefore is twofold. On the one hand, the sociologist is encouraged to consider the taken for granted aspects of everyday life, particularly with regard to engaging with risk and discounting personal attributes or experiences the individual brings to the risk situation. Social class, for example, is a powerful factor in this context. On the other hand, it is also important to analyse how institutions are organised and how individual circumstances and decisions are shaped by wider institutional structures. This facilitates a greater understanding of the ways in which human behaviour, in this case healthy volunteering in clinical trials, and regulation are produced and sustained by particular social norms, rules and types of actors (Walker et al. 2012). Using this approach

therefore means taking the conduct, organisation and regulation of FIHCTs as an ensemble of individual and institutional/technical aspects within established regulatory, ethical and socio-political systems and individual actions as well as socio-economic and socio-political contexts. The approach requires taking into account the fact that institutions are comprised of the "myths and visions that … capture the imaginations of its participant actors" (Avegerou 2004:3) as well as the subdued voices within and outside these structures and how the systems in place propagate and define social norms (Walker et al. 2012) and how they shape daily life experiences.

Thus, questions about motivations require consideration of not just individual reasons for actions but also that institutions have their own motivations, often described as interests, which drive their policies and approaches to business and are fundamental to the structure and functions of the institutions (Douglas 1987). For a long time organisations have been seen to be composed of production and exchange systems, with technological systems moulding their structures and their influence emanating from the interdependence of these factors. To understand how institutions operate, shape and view actors' experiences, the phenomenological approach to institutional theory requires greater attention to the significance of the symbolic facets of institutions. This is because institutions are not just technical systems; they also have an impact on the environments in which they exist (Scott, 1987) and on the individuals in and around them.

Rather than adopting a utilitarian perspective, which takes the premise that individuals always pursue their own interests, taking a phenomenological approach to understanding human involvement in clinical trials and regulation entails considering how individuals and institutions interact and refocuses attention on taken-for-granted factors such as norms, assumptions and social circumstances that delineate people's actions. This should not be taken as a disavowal of the reality of purposive actions by institutions or individuals but rather as a demonstration of ways in which people's actions are equally shaped and defined by interactions between institutions and individuals (Scott 1987).

2.7 Summary

This research is situated at the nexus of the healthy volunteering individual and the institutional nature of FIHCTs. It aims to examine how individuals and institutions interact to shape human involvement and to delineate conceptions of risk in clinical trials.

The theorisation of both healthy volunteering and institutions in this research is influenced by phenomenological approaches, particularly Schutz's concept of system of relevances. This framework provides an analysis that considers government and non-governmental regulation, corporate organisations and professional expertise and how they view individuals and bodies, and define customs and practices. This framework is useful because the business of FIHCTs takes place in a field of interdependent but varied organisations and actors. Rational consent, payments and trust, along with economic or gift exchanges, morality and biological citizenship are all ultimately dimensions of human involvement in clinical trials. This chapter has reviewed literature and discussed current research based understanding of how human involvement in clinical trials is shaped and influenced by both individual/subjective and institutional contexts. A phenomenological approach to the system of relevances can include institutions and offers a framework that is useful for identifying key actors and agencies and their relations, and the nature of fundamental principles that govern the institutions and practices of regulation of FIHCTs.

Research on healthy volunteering has demonstrated how the interplay of social, commercial and political contexts influences the conduct and experience of clinical trials but it has been carried out only in the US. Abadie's (2010) research on "professional guinea pigs" in an anthropological/ethnographic study explored ways in which anarchist groups and some HIV patients have made healthy volunteering a "profession" of sorts. While some research has acknowledged and incorporated institutional aspects on a global level, the focus has mostly been on emerging economies as sites of offshore clinical trials. There has been little research in the UK on healthy volunteering, where most of the focus has been instead on patients' involvement in medical research. For

instance, Featherstone and Donovan (2003) describe patients' understandings of their own participation in randomised clinical trials, Hallowell et al. (2010) discuss cancer patients' motivation for involvement in clinical trials and Corrigan (2003) researches patients' perceptions of informed consent in the clinical trial context.

The literature discussed in this chapter can be arranged into the following themes: ethics, the role of trust, the exchanges which take place in the context of healthy volunteering, morality and biological citizenship. The discussion in this chapter has highlighted the influence of economic and rational theoretical approaches to concepts of individuals as rational actors and surveyed the body of work on human involvement in drug trials globally. The literature shows that involvement in clinical trials is often reserved for those who are from poor or financially disadvantaged groups. Questions remain about the demographics and motivations of healthy volunteers in FIHCTs and the regulation of clinical trials and how they are structured and organised. The following chapter discusses the methods used in this current research.

Chapter 3
Research Methodology, Design and Methods: Exploring Human Involvement in Clinical Trials

3.0 Introduction

Chapter 2 examined the different theoretical perspectives that shape discussions on human involvement in clinical trials. It concluded by looking at how Schutz's (1970) phenomenological approaches – in particular his system of relevances – can contribute to research into ethical and regulatory issues in human clinical trials. However, before applying this theoretical framework to my research topic, I will explain how and under what assumptions this will be done.

The first part of this chapter outlines the philosophical stance on which this research is based. This is followed by a discussion of how the methodological approach developed. I then describe my experience of the sampling and recruitment of participants for the research. The next section discusses the tools used in the collection of data. I then outline the ethical considerations and discuss the challenges of doing research involving elite and multinational pharmaceutical corporations in terms of access and their desire to influence the research. I also discuss the challenges of researching motivation and its impact on the interpretation of findings. The chapter ends by considering the reliability and validity of the research. This chapter is both a personal and epistemological reflexive account of the research process. It outlines the rationale for the methodological approach for the research and gives an account of the factors that shaped the research process and, subsequently, the findings.

3.1 Phenomenological research

The theoretical framework adopted throughout this research into human involvement in FIHCTs is influenced by phenomenology, particularly Schutz's system of relevances. Unlike assertions in many studies about the need for rigour and objectivity in social research (Haslam

and McGarty 2003), using this approach entailed acknowledging and reflecting on how my role as a researcher influenced the research process and its outcomes.

The main aim of phenomenological research is to identify specific phenomena by looking at how they are viewed by the actors experiencing a given situation. This involves gathering "deep" information and views using inductive, qualitative methods such as interviews, discussions and participant observation. Findings are then presented from the research participant's point of view. Phenomenology, as discussed in Chapter 2, involves the study of individuals with particular emphasis on the ways in which everyday interactions become normalised, embedded in everyday culture, and thus taken for granted (Schutz 1970; Bloor 1995). From an epistemological standpoint, phenomenological research is grounded on the paradigm of personal knowledge and subjectivity that emphasises the importance of an individual's perspective and interpretation. Phenomenological research also investigates and exposes the chaos of everyday assumptions and conventional wisdom (Lester 1999).

In practice, phenomenology overlaps with other approaches such as hermeneutics, symbolic interactionism and ethnography. In a classic sense, phenomenological research is thought to be focused on describing rather than explaining phenomena without preconceptions, in the form of a hypothesis (Husserl 1950). But this approach is challenged by humanist and feminist researchers (Plummer 1983; Stanley and Wise 1993), who argue that social research cannot be done *without* any preconception or bias. Instead, they emphasise the need for a clear understanding of how meanings and interpretations have been made and how they relate to research outcomes. Instead of the researcher being a detached and objective player in the research, they argue, the researcher should be made visible within the "framework" of the research. In this case, a reflexive approach to research is recommended. Since I was in the same environment and principally engaged in collecting and interpreting knowledge, it was virtually impossible to ask questions of others, such as interviewees, without turning the analytical gaze on my own practices.

Arguably, social researchers cannot take a neutral stance outside the political, social and cultural customs of the people who are subjects in research (Abu-Lughod 1991). My research involved interacting with people from different cultural backgrounds and social status and I was made aware of my own status and ethnicity and of how they might shape my participants' responses to my questions. For instance, interviews with professionals were always formal and tense with the exception of those with ethics committee members. The interviews with healthy volunteers were relaxed and involved different power dynamics. I was also aware of how my own preconceptions and perceptions about the interviewees could influence my views of the subject. Most importantly, I took into consideration the fact that participants had had experiences, social circumstances and knowledge far different from mine. This meant that they were unavoidably "co-producers" of the knowledge in this research (Ansell 2001).

The phenomenological approach is used in this research because it is effective in exploring from an individual's perspective his or her experiences and views which may often remain unexpressed or taken for granted. In exploring professional and lay perceptions of risk, I draw on Husserl's (1950) approach to show how in given contexts the "other" is constituted and how individuals with a given set of resources and general rules use these to construct an "other". For instance, in relation to questions of risk professional and lay views mostly construe each other as, indeed, the "other" (Wynne 1996). The different ways in which people assess and experience risk and the "other" become clear when the views of professionals and healthy volunteers are juxtaposed and the context in which their interactions take place is analysed (Husserl and Moran 2001; Eberle 2013). Therefore, a phenomenological study that includes structural context was used. I took into account points of convergence and divergence between actors in different structural contexts or positions in the structural hierarchy (DiMaggio and Powell 1991) in order to reveal how risks are perceived and experienced. This made the approach useful in challenging structural and normative conventions. Furthermore, phenomenological research, when combined with an interpretive

dimension, makes it a practical approach, allowing it to be used to buttress and or challenge policy and even action (Lester 1999). Moreover, one of the strengths of a phenomenological approach is that, unlike some early forms of discourse analysis (Simons 1995), it does not just focus on understanding the participants' experiences and suggestions of resistance or how they construct their identities; rather it provides an agenda for change by considering how research can "help" people or implement change and inform a progressive social or policy agenda (Creswell and Clark 1999; Bloor 1995).

Although I have emphasised the need for reflexivity, it is also true that there is value in data gathered in an unreflexive manner; this may bring about fruitful results, for instance, from questionnaires or even the simple conversations with which I started the interviews.

However, phenomenology has been criticised about the generalisability of its findings. Unlike positivist research, phenomenological research findings cannot simply be generalised to the wider population (Bryman 2004). Therefore, the use of individual subjective accounts in my study means that this research cannot be generalised. However, as Flyvberg and Stake argue separately, despite the unique nature of each account and experience, each may be a part of a wider consensus and thus could be used to think about how others in similar situations may be experiencing life (Flyvbjerg 2006; Stake 2003). For instance, considering how healthy volunteers become involved in clinical trials could be used to develop ways in which the recruitment of and sharing of information with participants in medical research could be improved. This is not to suggest that the findings from this research could be generalised to all clinical trials or healthy volunteer experiences. Also, as Flyvbjerg (2006) and Yin (2009) state, findings from qualitative research can be combined and expanded into wider theories. Insights from qualitative research can also prompt the development of quantitative tools which could establish whether the qualitative findings are generalisable. Therefore, this study could contribute to theories of human involvement in medical research and could be relevant in the conduct and regulation of future drugs trials involving

human volunteers. Nonetheless, the idea of generalisability based on statistical conceptions is obviously not applicable here. In the following section I discuss how the methodological approach used in this research developed and evolved.

3.2 Developing my research approach

"Method is journey after one has travelled it" (Ginzburg 1993:1). This assertion resonated with my experiences while doing this research. The initial research design was a sociological ethnography involving observations, semi-structured interviews and documentary analysis. The justification for this was based on the approach of Layder, who argues that using a combination of such qualitative methods in this manner is an effective way of collecting data as it happens or shortly after it happens (Layder 1994). However, in response to changes in the field I decided to use a questionnaire as a tool for data collection.

The influence of space and place on the design and process of social research has been extensively discussed (Massey 1992, Bryman 2008). Of particular relevance for me was the question of how research involving professionals, corporations and people in positions of power can influence how social research is conducted. Bryman (2012) argues that social research in corporate settings is particularly prone to influence because of funding and access issues, which researchers must negotiate in order to conduct research. It is possible for funders, specifically private funders, and gatekeepers to push for research to be done in a certain way and for questions to be asked that might differ from what the researcher intended (Walford 2011).

My initial plan was for a qualitative study with observations of clinical trials in progress. My observations were intended to aid exploration of the regulatory policy implementations and practices. However, encounters with corporate gatekeepers to negotiate access changed, as they made clear that they would only support the project if it were a quantitative study:

> [T]he only way to do this project is for you to prepare a questionnaire that would be sent out to all those on our register, that's all. No such thing as interviews, no one will talk to you considering the numbers you want (Corporate Professional 2).

> I doubt there will be anyone one willing to talk to you; this is a complex industry and obviously ethical issues will make it difficult for anyone to give you access as well as let you observe. We need the approval of the sponsors. I would suggest you use questionnaires … for your study (Corporate Professional 12)

In these extracts, the gatekeepers felt qualitative techniques were not an ideal approach even when the rationale for the method was explained. They believed the only way to do research was to use survey questions. It is possible that using surveys was not about developing the best technique for data collection but rather about a type of research that they would possibly find more convenient, but this would mean that certain questions would be asked and answered to a limited depth while other questions would not be asked at all. It was also apparently preferable to have me on the premises for a defined period instead of "hanging around" (Gold 1958; Kawulich 2005). The private nature of the business meant that as an outsider I was likely to be viewed suspiciously, possibly even as a spy (Adams 1999) or a journalist. All this could have added to their apprehension. Because the gatekeepers had such strong views about research methods, after some negotiation I drafted a questionnaire as a data gathering and recruitment tool. I argued that interviews would add to the research outcomes while quantitative responses would strengthen the arguments and provide scarce statistical data about healthy volunteers.

I was not permitted to observe phase I clinical trials in progress except for a 30-minute observation which was strictly supervised and which failed to yield sufficient data. It was, however, useful in demonstrating how difficult it is to conduct research in such settings. After further negotiations, the questionnaire was used only for recruiting volunteers as interviewees, but not for the professionals. With the use of

questionnaires, observations were eliminated, my main research data collection tools became mainly interviews, and documentary analysis was supplemented by statistical data. The questionnaires provided unique demographic and other data for the research. Using a mixture of data collecting tools in social research is widely supported as a more responsible and comprehensive approach to doing social research (Bryman 2012; Coxon 2005). Combining qualitative and quantitative data allows for analytical triangulation in which a subject can be investigated by three methods (Bloor 1997).

3.3 The development of qualitative research

Qualitative research methods have been part of social science since the early 20th century. Of particular significance was the development of the Chicago School of Sociology in the 1930s. During this period there was a departure from the tradition of doing research by following the conventions of the natural sciences. It should be mentioned that the debate about ways of doing social research had been ongoing and would continue into the 1950s and beyond. This resulted in a desire to explore social phenomena that could not be investigated using conventional methods (Hammersley 1989). These developments, coupled with advances in anthropological research by Malinowski and Mead among others, led to the possibility of establishing and justifying qualitative research as we know it today (Bryman 2004; Silverman 2010). Denzin and Lincoln define qualitative research as "multi method in focus" and involving the studying of "things in their natural settings, attempting to make sense of or interpret phenomena in terms of meanings people bring to them". It also involves using "case studies, personal experiences, introspection, life story, interview … observational, historical, interactional and visual texts" (Denzin and Lincoln 1998:3) as sources of data.

Qualitative social researchers must be able to account for their role in the research process. In contrast to quantitative research, which focuses on objectivity, qualitative research concerns itself with parity in the relationship between researchers and participants, or at least some

understanding of the relationship if parity is not possible. There is a recognition within qualitative research of the influence this relationship has on research outcomes. There should also be an acknowledgement of the potentially exploitative and intrusive nature of the researcher-participant relationship and its impact on the production of data (Reinharz and Davidman 1992; Adams 1999).

3.4 Sampling: recruiting participants for the research

Sociological research most often involves groups and institutions. The research often starts with the identification of the interest group or institution followed by the development of a strategy for accessing participants in that context (Flick 2009). However, the definitions of a "healthy volunteer" are ambiguous, and identifying a group of healthy volunteers found in one place was not possible. Identifying professional participants proved difficult too, as they are able to protect themselves from public access by complex gatekeeping strategies. This challenge was overcome only after a number of failed attempts.

To access healthy volunteers, I contacted several CROs whose details I had found on the clinical trials accreditation scheme of the MHRA. About 20 e-mails were sent to operations managers or others in authority. Five replied that they were not in a position to help me to access healthy volunteers. Two were willing to discuss this further. One agreed to help provided I changed my approach to include the questionnaires mentioned above. Working with his CRO I agreed to sending a questionnaire to healthy volunteers to recruit participants for my research. The outcome was a non-random sample survey with 187 respondents, of whom 97 agreed to be interviewed. This yielded 25 interviews. Contacts provided by four of the respondents led to a further 10 interviews.

Recruitment of professionals working for CROs involved, first, the e-mails seeking access to healthy volunteers. I requested an interview with the five recipients who responded, or any of their staff. Four declined. I decided to adopt a different approach. I searched clinical trial forums for contributors, looking at what they wrote and where they worked. I

redrafted my research synopsis by personalising the summaries and, where possible, citing them. This proved fruitful and within a few days I had secured agreements to be interviewed from a medical director and an operations manager of one of the units. This allowed me to conduct three interviews with professionals. One interview was over the phone; the others were face to face.

Research ethics committee participants were selected from a list of ethics committees available online on the Research Ethics Service website, which contains details of committees dedicated to reviewing applications for FIHCTs and contact details of the chairpersons' assistants who could arrange meetings. Five e-mails were sent to ethics committees in London that review FIHCTs. One participant agreed to an interview over the phone; another agreed to be interviewed face to face. Two other ethics committee members were recruited at a conference I attended. A member of the Association of the British Pharmaceutical Industry (ABPI) was recruited after I had e-mailed the head of the organisation. The member of a team that specialises in FIHCTs called me to arrange an interview. As for professionals from the MHRA, I was able to interview the director of a team who gave his permission for three other interviews, two with members of his team and one with a member of another division. I arranged a total of 47 interviews – 12 with regulatory officials and corporate professionals and the rest with healthy volunteers. Table 3.1 on the next page is a summary of participants used in this research.

Participants	Survey Respondents	Interview participants
Healthy volunteers	187	35
CRO & ABPI Corporate Professionals	-	4
MHRA Regulatory officials	-	4
REC Regulatory officials	-	4
Total Numbers	187	47

Table 3.1: Summary of research participants

The sampling framework used in this research was purposive and snowballing (Bryman 2012). This was ideal, as it was difficult to find the subjects – especially healthy volunteers – in one place. The challenges of accessing professionals meant that snowballing became the most appropriate approach in finding participants.

3.5 Data collection

This section describes how data were collected and the challenges encountered in gaining access to participants.

Documentary analysis

The study design included an analysis of documents. According to Prior (2003), analysing documents can provide an insight into how organisations operate and is a source of information for interviews. The purpose of my documentary analysis was twofold: first, to develop an understanding of the regulatory context in human clinical trials, which involved exploring regulations regarding rewards, risk management and mitigation in general; and second, to inform subsequent interviews, which enabled me to understand what information was in the public domain and helped me to formulate appropriate questions for professional and healthy volunteer participants.

I made systematic searches for relevant scientific and regulatory literature and, where possible, reports held by organisations. The documents analysed were mostly those found on organisational websites such as the Medicines for Human Use (Clinical Trials) Regulations 2004[3]. The analysis included a comprehensive review of guidelines and procedures for the regulation of clinical research organisations and how they were interpreted (Prior 2006). It also involved the study of documents given to volunteers prior to consent, such as information sheets and consent forms (Corrigan 2003). Among the documents analysed were Department of Health and EMA reports of the 2006 Northwick Park incident.

[3] (National Archives: www.legislation.gov.uk/uksi/2004/1031/contents/made).

The documentary fieldwork involved a qualitative content analysis, identifying and listing themes from regulatory documents, monitoring the implementation of regulatory guidelines regarding drug safety, risk, informed consent and incentives, in order to develop a broad picture of the issues to be investigated (Abraham and Reed 2001; Abraham 1994). This was important because, as Abraham (1994) states, it led to analysing institutional technical inconsistencies and their underlying values, and the practical implementation of regulatory frameworks. The role of documentary analysis in informing interviews (Bryman 2004) was clear in this project; for example, interview questions on payments, safety and professional concepts of risk were prompted by documents I had read.

However, accessing documents was challenging because I was dealing with multi-national pharmaceutical corporations as well as government departments which were not willing to reveal information that might generate negative publicity (Abraham 1994). As a result, the documents I analysed were only those available publicly or those that I requested through the Freedom of Information (FOI) Act (Bryman 2004). Documents that I expected to find turned out not to exist. For example, to find out the number of clinical trials that were cancelled due to "unexpected adverse effects" between 2006 and 2012, I made an FOI request. It took approximately three weeks to receive an answer from the MHRA. The request generated the following response:

> Dear Mr Mwale
> REF: FOI 13/608
>
> During the period December 2006 and December 2012 we had no reports of First Time in Human (FTH) trials being stopped due to adverse event.
>
> If you have a query about this letter, please contact me. If you are unhappy with our decision, you may ask for it to be reviewed. That review will be undertaken by a senior member of the Agency who has not previously been involved in your request …

Considering the number of FIHCTs that take place every year in the UK this response was baffling. During the study, accounts of volunteer experiences in trials that were discontinued because of unexpected side effects were common. Healthy volunteers talked of being sent home from a trial in the previous two years. Either regulators do not keep such records or if they do, they are not willing to make these public. I had also hoped to access documents relating to information given to volunteers for studies, but these were provided only on request to people interested in taking part in a particular trial or to people who registered an interest in volunteering with a CRO. I therefore registered with several CROs, which have since sent me information when they are recruiting for a trial.

Studying only the documents that were publicly available limited the depth of the analysis I was able to conduct. Understanding how regulations are implemented requires analysing not only what guidelines are in place but how useful they are in achieving the desired goals – in this case, the safety of participants as well as systems of safety and organisational failures that result from differing interpretations of policy and guidelines (Bosk 2005). However, the use of different sources of data meant that such issues were explored in other ways. For example, questions about policy implementation were asked of professionals and in most cases they provided illuminating responses.

Despite these limitations, the documents accessed for this research proved to be useful resources for informing interviews. The information they yielded also shaped the discussion on regulations in the first substantive chapter of this thesis, which discusses the nature of the regulatory approach to FIHCTs.

Development of questionnaires

I approached the notion of creating a questionnaire mindful of the need to work within established conventions when conducting social science research, particularly because I take a phenomenological approach that is known for being qualitatively and not statistically oriented. The long-standing oppositional stance between qualitative and quantitative

"purists" (Ratner 1997; Adams 1999) obscures the potential merits of data obtained from survey and interview approaches and from the different contexts in which tools for collecting data are used. The limitations of using exclusively qualitative or quantitative methods have also been well documented (Bryman 2004; 2012). Disregarding research results simply because of the data-collection methods might result in the loss of vital insights. Statistical and narrative data are complementary in providing in-depth analysis and understanding of social issues. The use of questionnaires with open or closed questions in qualitative research is known to be of great benefit (Bryman 2006).

The methods used in the study involved a mixture of tools – semi-structured interviews, document analysis and a questionnaire survey. Interviews and documentary analysis were the main tools for data collection and were supplemented by the quantitative survey data. The triangulation of quantitative survey data, documentary analysis and interview data was intended to bring about an in-depth understanding of the subject (Olsen 2004) and not merely to deal with validity or trustworthiness issues (Hamersley 2008). As mentioned, the original research design did not include questionnaire surveys. Questionnaires were introduced as a recruitment tool and were sent by the gatekeepers to prospective participants listed in their register of healthy volunteers.

The need for questionnaires prompted me to think about the demographic profiles of healthy volunteers: educational attainment, age and occupation, etc. Such data are kept by CROs and are not made available for public use. Healthy volunteers are usually seen as unemployed or poor (Fisher 2007; Abadie 2010) according to profiles of participants gleaned through qualitative research. For this project, questionnaires were also useful for informing the interviews that I would conduct. To ensure that the questions were appropriate, I drew on crime and health surveys of the Office of National Statistics that offered data about employment and attitudes. My survey was developed in July 2012 and was piloted in August 2012 among University of Sussex students who were available at the time and because I did not have direct access to the potential respondents. The

survey was revised after consultation with the initial respondents as to the clarity and effectiveness of the questions. The questionnaire was developed in a very short time because the gatekeepers wanted it sent out within two weeks of our meeting. I also had to wait for a supervisors' review and ethical approval for changes to my research methods. Dealing with such challenges was stressful, but I had to take care not to lose the confidence of the contacts.

My contact at one CRO sent the questionnaire to about 80,000 registered healthy volunteers on its books in mid-September 2012, about two months after our initial contact. Regarding the population from which the survey sample for this research was drawn, it must be noted that 80,000 was a number given to me by my contact. I could not verify the claim, so while the number may be accurate, it is possible that the number may well include patients they have registered to take part in clinical trials or indeed potential healthy volunteers who may have merely expressed interest to take part but have not been involved in any clinical trial. Therefore, this figure must be taken with caution. Nonetheless, using this sample and data it generated it was still possible to conduct an analysis and obtain meaningful insight into the demographic profiles and attitudes to risk of some healthy volunteers in the UK.

I began to receive data from the questionnaires in November 2012. A total of 187 respondents took part in the survey (see appendix 2) and the positive response was by far the most important step in gaining access to healthy volunteers for the second part of this study – the interviews.

The questionnaire was important in other ways. Being the first such survey in the UK among healthy volunteers, it provides an overview of the demographic profiles of healthy volunteers involved in clinical trials in the UK. The limitation of this approach is that it is based on a non-random sample and thus it does not represent the wider healthy volunteer or professional populations involved in FIHCTs because the participants were selected on the basis of availability. However, it drew on a register claimed to include more than 80,000 healthy volunteers (see above point

about this number) of a well-established CRO. Moreover, only those participants who had access to the Internet were selected for the study. According to the Office of National Statistics (ONS), 73% of the British adult population accessed the Internet every day by 2013; 72% of those aged 24–35 were more likely to use the Internet; for the unemployed 67% had used the Internet for job applications. It is not clear where they accessed the Internet, and it is possible that people without Internet access who take part in clinical trials on a regular basis were omitted from the study. Therefore, it may be difficult to draw wider conclusions about the demographic profile of healthy volunteers.

The survey was useful in that it allowed for a comparative analysis of the motivations of healthy volunteers in the UK and substantiated their social context in terms of income, employment and levels of education. Consequently, it became a foundation on which to build the qualitative aspect of the study. The survey revealed surprising differences in age and income levels, with many university graduates taking part in clinical trials in the UK.

The questions explored healthy volunteers' views of aspects of the clinical trials and their perceptions of risk. They were asked to consider hypothetical situations relating to payment – for instance, how likely was it that they would take part in a five-day FIHCT that would pay them £1,000? This opened up the possibility of exploring their perceptions and experiences in negotiating risks at greater depth. Moreover, responses to the questionnaire tended to be positive presentations of selves. Thus, the questionnaire became crucial in informing qualitative interviews. It was clear that most participants had paid more attention to issues of rewards and risk in clinical trials and less to altruism; this emphasis was reflected in the time spent exploring these issues in the interview.

The contact details provided in the responses proved to be crucial: I e-mailed all 97 participants who had agreed to a further interview and asked for a meeting at their convenience. Though it is uncommon for phenomenological research to include questionnaire surveys, social science research uses questionnaires for data collection by way of open-ended or

even closed questions. Such tools help to gather data beyond that collected by interviews or observation tools (Woods 1998). Therefore the use of the questionnaire in this research added to the depth of qualitative data and the credibility of research claims. For instance, challenging assumptions that healthy volunteers are poor, work-shy or uneducated, the survey found most of them to have a high level of education and while they may have jobs, for one reason or another they feel forced to become involved in clinical trials.

Semi-structured interviews

Building on the statistical data and documentary analysis, the other aspect of the study involved interviews. It has been observed that when well used, interviews are useful in exploring issues that people talk about only if they are probed (Reinharz and Davidman 1992; Willig 2008). Therefore, interviews are useful in exploring deep-seated values and beliefs. They also provide an opportunity to deal with people's tendency to present themselves in a good light when questioned about sensitive or private subjects. In this way, researchers can follow up on issues that spontaneously arise during conversations or rephrase a question to get to the heart of the matter (Atkinson, Coffey, and Delamont 2003; Coffey and Atkinson 1996).

All the interviews for this study were semi-structured and aimed at recording the participants' histories, experiences in the clinical trial process, motivations for taking part in clinical trials and perceptions of risks. In addition, I wanted to explore how their different individual positions, decisions and relationships intersected with wider medical discourses, cultural beliefs, customs and socio-economic circumstances, and how their participation in clinical trials affected them in the course of their involvement and beyond (see appendix 1 for interview schedule). In doing so I hoped to avoid the common trap of presenting people's experiences as homogenous and internally coherent (Abu-Lughod 1991). Instead of producing a smooth narrative about risks, rewards and the regulation of clinical trials, including questions about personal histories in interviews was useful in revealing the contradictions, conflicts and moral dilemmas people

face in their daily lives. It is out of these dilemmas and – possibly more important – the participants' attempts to negotiate them, and the regulatory and research organisations' attempts to mitigate against risks, that the "risk, rewards, regulation and ethical dimension" in the title of this project emerged.

The interviews were approximately 45–60 minutes long. They involved a variety of questioning techniques with a combination of specific/general, open/closed questions aimed at eliciting factual or "hard" data and "soft" data (Willig 2008; Gillham 2000).

I conducted four interviews with regulatory officials, incumbent or former serving members of RECs. One was by telephone; two were conducted in the officials' offices and one during a lunch break at a conference. For regulatory officials working for the MHRA, interviews took place in their offices. For corporate professionals working for CROs, two interviews were conducted at their premises while one was done by telephone. A further interview was conducted with a representative from the ABPI. In all cases, interviews took place at a time and place convenient to the participants. The difficulties in gaining access and the defensive and sometimes aggressive attitude of professionals in institutions in which I did not feel at ease made me nervous and self-conscious.

Interviews with healthy volunteers took place face to face, over the telephone or Skype, or in e-mails. Face-to-face interviews were conducted with 20 participants in public places such as restaurants and cafés close to where they lived and at times that were convenient for them. Meetings and venues were arranged via text or e-mail. I was worried – needlessly as it turned out – that the participants would find it difficult to talk in public places about their experiences. Some of the participants talked at length about their experiences and were keen to share them. They seemed to be at ease with me as a researcher and it was usually easy to direct the interviews – a contrast to the challenges of interviewing professionals. Most of the participants were from London and the south-east, including Kent and parts of Hampshire. Ten participants were interviewed over the phone, including four in Scotland and Northern

Ireland. Another six interviews where done over the phone because of the participants' work schedules. Three interviews with participants in Brazil, India and Sweden were conducted via Skype. A further two interviews were done via e-mail at the convenience of the participants, who were abroad.

Using a semi-structured interview approach was of great benefit as it afforded me the flexibility of a "loose" interview schedule for the fieldwork and with individual interviews (Willig 2008; (Shipman 1997). Participants felt able to raise matters of importance in their experience as professionals and lay participants in medical research. The semi-structured interview allowed the participants to cover broad areas that I was interested in exploring. At the same time, it also allowed me to direct conversations to some extent. Using a combination of interview techniques, I was able to give participants time to share their experiences at the times when they were most comfortable and did not feel rushed (Holt 2010; Sturges and Hanrahan 2004).

Conducting interviews by telephone and Skype meant that I was able to deal with the challenge of time and space that would have arisen had I restricted myself to face to face interviews only. The advantage of using Skype and telephone interviews was that participants were afforded more confidentiality (Hanna 2012; Hanna and Mwale forthcoming). The use of Skype requires a good Internet connection. In one interview a poor connection disrupted the interview and I found myself talking over the participant's responses. I apologised frequently and was concerned that the interview came across as unprofessional; it was longer than I intended. Using the telephone meant that I could not read the facial expressions and body language of the participants. To make up for these limitations, I clarified confusing parts of the interviews in e-mail exchanges. I also exchanged e-mails with participants with whom I had conducted face-to-face interviews. Willing participants in research are likely to give open and genuine accounts of their lived experiences (Shenton 2004), and this meant that the study became a rich source of data about the experiences of healthy volunteer and professionals and their views of FIHCTs.

A limitation of this research is that the interviews were conducted at a particular point in time; hence the study was cross-sectional rather longitudinal. Such data do not tell us how healthy volunteering started and developed over time. To address this limitation, participants were asked how they came to be involved in clinical trials. This was useful in exploring the historical dimension of their involvement and the contradictions and moral dilemmas that participants negotiate when involved in clinical trials.

Access

As mentioned earlier in this chapter, a major challenge of this research was finding and accessing participants. Getting access to multinational corporations proved to be a complex and lengthy process. Like other institutions, pharmaceutical companies, regulatory bodies and CROs have rules and gatekeepers. CEOs must consider the needs of investors and shareholders must be considered. CEOs are entrusted with maximizing dividends for their businesses (Rajan 2007) and may make initial decisions about whether a researcher should talk to employees and or volunteers (Buchanan and Bryman, 2007). There is a culture of secrecy within these organisations (Petryna 2009) and such hierarchical systems require negotiation with professional teams involved in the administration of clinical trials; they have other demands and interests and they all work amid complex power relations (Ansell 2001, Foucault 1980). Negotiating with such a diverse group of professionals requires flexibility and patience. Furthermore, negotiating access and consent did not only involve institutions, but individual healthy volunteers as well. This was particularly important for this research as it involved individual participants who were to share their stories (Barker and Weller 2003).

The secrecy that surrounds the practice of clinical trials raises an important question for researchers: is it possible to carry out research transparently when one's informants are not open and transparent? Secrecy in biomedical research is in sharp contrast to postmodern social research practice, in which the social production and distribution of knowledge is regarded as being key to solving social problems. In overcoming the hurdles thrown up by secrecy, I drew inspiration from similar research on

later-phase trials undertaken by anthropologists Fisher (2007), Rajan (2007), Petryna (2009) and Abadie (2010) and the sociologist Corrigan (2003). All had managed to access participants in different ways and settings.

Negotiating access

Central to the British Sociological Association (BSA) research code of ethics is the principle of transparency. This is also emphasised in literature on postgraduate research. It is vital that participants are well informed and are given a clear explanation of what is expected of them in the context of the research and the purposes of the research (BSA 2004; Bryman 2012). Gaining access to elite and corporate organisations for this research was challenging as they can readily deny access and keep themselves beyond reach and scrutiny (Duke 2002). In my research, gatekeeping took different forms, for instance involving personal assistants who needed convincing to grant access to their superiors and in one case a chief executive who had to sanction a meeting. When e-mailing them to ask them for access I received an unexpectedly high number of rejections and non-replies. The replies were similar. One e-mail read in part:

> thank you for your e-mail and the questions, they are interesting and insightful. After discussions with my team, we have decided that we do not have capacity to attend to guests such as yourself at our facilities. Besides, the questions you are proposing to ask are what we already ask our staff and volunteers …

Discussions in research methods literature about access to professionals sometimes overlook the fact that the researchers may have no prior contact or relationships with organisations. Negotiating access for this study was extremely problematic. As time was running out and access had to be obtained one way or another, I changed my approach. More potential participants were identified via the professional networking site LinkedIn and in some cases institutional websites. The selection was based on job titles and roles in the industry, including those involved in administering, managing or running clinical trial units. A further search on

their publications and interests was carried out and project summaries were rewritten to pique their interest or highlight subjects they had written about (Thomas 1993; Duke 2002). These personalised summaries were more successful in obtaining access to professionals as the following extract of an e-mail shows:

> Thanks for your e-mail. I would be happy to talk to you about my experience of working with healthy volunteers in first-in-human clinical trials … I suggest that you might telephone me on the number below, at a time that suits both of us. Currently, I can offer the following…

Accessing healthy volunteers was also challenging. Requests to prospective participants to e-mail, text or call to arrange interviews were not always successful. Due to the time that had passed between completing surveys and arranging interviews most of them had forgotten having taken part in the survey and needed reminding; access had to be renegotiated. One participant remained unclear what the research was about although she had been given the necessary documentation. She was sceptical about who I was and how I had obtained her details. We exchanged over 15 e-mails before she agreed to be interviewed. Later I found out that recent experiences in her personal life made her wary of people she did not know, especially if they were interested in her story. Others who initially agreed to be interviewed declined further interviews or did not respond to my request for meetings. Access to healthy volunteers therefore was not always straightforward despite having a contact list.

Influence of professionals on research questions

In Section 3.2 I discussed gatekeepers for this research who were influential in challenging and changing the methods used in this research. They insisted on the use of questionnaires, influenced the questions I was to ask the participants and even wanted to control the interview schedule. They asked to see questions in advance and demanded that some questions

relating to risk, safety and rewards, for instance, should be omitted both from my interview schedule and questionnaire. This was one response:

> we do not deal with uncertainty and risks in our work. We are sure of what we are doing. So you are not asking these questions [about risk and how much volunteers are paid for taking part in clinical trials]… alright?" (Corporate Professional 1)

This was not a request but an outright command to change my interview schedule not to focus on questions of safety and uncertainty. The gatekeepers also influenced the way the data were collected, declaring who would be involved, where, for how long and what information they would give me. One wrote me:

> Thank you for your e-mail. I have been clear that there will be no contact with volunteers without our supervision. The interviews will be over the phone lasting no more than 15 minutes and we will provide the space and telephone for you to use. You will not be given their contact details nor will they be asked to give them to you … (Corporate Professional 2)

To conduct research in in the face of such attitudes requires perseverance, imagination and flexibility. Although I had reservations about their suggestions, I decided to comply with their demands. After collecting data from the questionnaires I was given contact details to arrange the interviews myself rather than follow their suggestions.

Rapport building and the "corporate line" as hurdles

Another problem was building of rapport. Research ethics guidelines and training emphasise the need to build rapport with participants to elicit their trust and develop an understanding (Kvale 1996; Bryman 2012). In practice this was extremely difficult. I found that in these settings there was no time for rapport building; the people I met were abrasive and uninterested in the researcher and the research. A typical beginning to most encounters was: "I am very busy and only have 15

minutes so let's cut to the chase. What can I do for you?" Or "I am sorry, I forgot you were coming. Can we rearrange to meet next week?"

The interviews took place on their premises – places which were alien to me – adding to the intimidating atmosphere. In response to questions about views on practices – for instance, informed consent and calculations of rewards to volunteers – participants took a combative or dismissive approach. Some tried to dictate the terms on which the research was to take place. Others tried to put me off by not answering questions or diverting the focus of the interview to other questions or talked down the significance of my study, as seen in this extract:

> Who are your supervisors? … I must say that if they had any idea about ethics and how the industry works they would have advised you not to embark on this journey. What I am saying is that this project is not possible. No one, I repeat no one, will talk to you or answer any of the questions you are asking. I am doing you a favour to save you from … heartache in future… (Corporate Professional 12)

This quote illustrates the influence powerful individuals have when involved as participants in social research. They are the producers and guardians of discourses and systems that are being investigated will go to great lengths to protect the systems (Fitz and Halpin 1994), resulting in interviews yielding standard corporate responses rather than the participants' own views. One participant warned that if I would not get any professionals to participate in my research unless I solicited their official views. In four instances, participants insisted on talking off the record despite assurances of anonymity. Though this left me free to ask questions, they still took the official line and their responses were not particularly different from those of others. In fact, some things they said were actually public knowledge. As Thomas (1993) observes, it was important for them to feel assured that their jobs would be treated as sensitive and not threatened, and thus they would agree to the interview. Other participants seemed happy to share their observations and experiences.

When I succeeded in getting them to talk, some participants working for MHRA, CROs and the ABPI wanted to know how much I knew about their work and the politics surrounding the subject I was investigating. I must admit that I had a lot to learn from them. Duke (2002) observes that some professionals want to talk to someone they believe they can educate. I frequently found myself having to determine the degree of knowledge I should reveal. In some cases I endeavoured to be seen as knowing and in other cases to be seen as naïve. Sometimes this worked but sometimes it backfired. In one instance I was asked if I had read the history of the changes of the Medicines for Human Use Act in reference to FIHCTs. My initial assessment of this encounter was that my participant would have liked to educate me about things so I decided to present myself as "naïve". To my surprise the participant said I had some homework to do before I could go around asking questions. This prompted some quick backtracking on my part to explain that I did not quite understand the question. Another experience in building rapport was that I often had to wrestle for control of the interview as some professionals tried to usurp the interviewer's role. This was awkward but after some subtle replies to their questions I would attempt to reclaim the role of interviewer. In these experiences it was frustrating to have been unable to express my knowledge and even my opinions for fear of being denied access or having an interview terminated.

These experiences were in sharp contrast to my encounters with professionals in public institutions, who were mostly ethics committee members, and with healthy volunteers in general. They were keen to have discussions about the topic and answer my questions. In some cases they offered to help me by talking to others in the industry to see if they could participate in my research. For civil servants knowledge production is seen as a public good while for professionals in private corporations it is a personal good that should be kept private (Stiglitz 1999). The latter wield a certain power and control over aspects of knowledge, making it difficult to scrutinise them and their activities.

Interviewing professionals: entering another world?

> To get to the office building from a bustling Victoria station, one has to negotiate and duck the many bodies in the way, put up with the noisy traffic on the streets and avoid one or two charity fundraisers. This is an ivory tower, you know. (Corporate Professional 1)

Professionals, especially those working in corporations, are visible to an extent. Their names are on company websites; they are sometimes in the media and nowadays are often present on online professional networking sites. They often work in modern buildings that are usually tall, often iconic and sometimes made of see-through glass. However, as Thomas (1993) observes, visibility both in the media and in buildings does not necessarily mean that individuals and their corporate activities are accessible. Accessing corporate premises is difficult. There are security scanners, security guards and receptionists to get past, and the host comes to receive you.

The quotation at the beginning of this section shows how corporate professionals view outsiders who come into their premises to ask questions. They inhabit an ivory tower of sorts, a term often used to describe academics, with the outside world as a nuisance that should be barred and kept out at all costs. This insider-outsider dichotomy is the basis of all encounters one has with professionals in these settings. The research encounter is a power relationship between the researcher and the participant (Scott 1984; Hunter 1993), which is explicitly demonstrated in research involving professionals (Ball 1994; Maguire and Ball 1994). Fitz and Halpin (1994) state that the power of professionals is even more evident when research has to take place in their offices, which might be intimidating to some academic researchers. Encounters with professionals in their offices also demonstrate how they shape the discourse regarding the subject being explored. They define the terms and what is said and known outside of the walls of the corporate headquarters, and this constrains corporate interviews. One participant, asked if it was possible to

talk to others on his team about their experiences and views, said I would gain nothing new, as illustrated in this quote:

> I have no idea why you think talking to more people in my team will give you more information; what I will tell you is what everyone else will tell you in my team. So there is no need to talk to more people (Regulatory Official).

Doing research with professionals involves negotiating not just the physical barriers of access but also official systems. At the end of each interview I would ask my participants for names of people they thought were important for me to interview. In only one occasion did this question yield a positive response. Some professionals inhabit tightly knit communities and will shield each other from public scrutiny. They may even conceal from colleagues that they had participated in an academic research project.

The irony here is that some corporate professionals would be very vocal and visible in the media about the need for transparency, yet they are not transparent with information or willing to answer questions about their practices. For early career researchers (ECRs) it can be a daunting task to gain access to professionals. Unlike established researchers, ECRs are likely to have limited social capital to facilitate access to professionals in corporate settings (Bourdieu 1985; Thomas 1993). Even established social science academics rarely conduct research among powerful corporate professionals. There is a valiant tradition, but it amounts to a tiny fraction of research energies and budgets.

What I found useful in these settings was identifying who wielded the power. Some members of organisations may not be actively involved in decision making, so identifying and accessing those who are at the core of the system is vital. In one case I contacted the operations manager of the unit rather the doctor who was conducting the trials, and I was directed to someone helpful. Because the request had come from the manager, I was treated with respect even it failed to get me an interview. Professional

participants are usually interested in knowing whom else you have spoken to (Duke 2002). In some cases I would decline to give names, citing confidentiality; the participants believed they could trust me with information and agreed to an interview. Most professionals wanted to know what they would gain from the research considering the amount of disruption I would be causing to their organisation. In one case I offered to help with a process review for the organisation's admissions and recruitment systems. Offering to give something in return for their participation seemed to ease their apprehensions about giving me access.

3.6 Data analysis

The quantitative survey data were analysed using SPSS software (Pallant 2010). The analysis involved simple tests, including descriptive statistics, frequencies and cross-tabulations. The questionnaire was designed with little time to consider possible tests that could be conducted on the data; hence it was difficult to do advanced tests.

A thematic analysis approach was used for the qualitative data gathered through interviews and documentary analysis. This method, which involves "identifying, analysing and reporting themes within data" is further used in interpreting various facets of the study (Braun and Clarke 2006: 79). This approach is useful because, unlike discourse analysis, for instance, it is not attached to any theoretical framework and thus can be applied to any approach depending on the aim of the study (Braun and Clarke 2006). One of the requirements of thematic analysis is that the researcher does the transcription, allowing for closer acquaintance with the data for preliminary analysis.

The first step was to transcribe all interviews verbatim; this helped me to understand the data and do a preliminary analysis. Four participants – three regulatory officials and a corporate professional – refused to have their interviews recorded; instead, I took notes during and after the interviews. All of the interviews for healthy volunteers were transcribed; those conducted via e-mail were already in text form. After transcribing, the data were uploaded into NVivo, computer software which is useful for

analysing qualitative data and arranging them in themes. The transcription phase had allowed for the identification of initial themes and using NVivo more themes were identified and added to those identified in the earlier phase. The interview transcripts were analysed for certain patterns and to categorise and organise the data into initial themes (Kvale 1996; Frith and Gleeson 2004). These reinforced themes identified during the transcribing phase. Thus, this first stage was an exploratory analysis of data. The second phase involved further analysis of the themes and focusing on convergences between themes. This was undertaken to ensure a greater understanding of the issues and to develop links between themes. The final stage involved looking at the themes in relation to the research questions and theoretical approach of the research to identify how they could be organised further to address the aims of the research (Gordon, Holland and Lahelma 2000; Lahelma 2002; Raisborough 2006).

The challenge of investigating motivation

The methodological challenge of researching motivation, particularly in semi-structured interviews, is that it requires participants to reflect on things they are doing or have done in the past in a rational way (Giddens 1984). Until the interview, motivating factors may be indistinguishable from customs, entangling motivation with taken-for-granted, everyday life events (Giddens 1984; Schutz 1970) and consequently difficult to explore in social research. Therefore, as Zigon (2007) observes, it is only when people come up against a moral dilemma that they become aware that they have to answer questions such as "Is it worth the risk?" It is when "people or groups of people are forced to step away from their unreflective everydayness and think-through … work on themselves and respond to certain ethical dilemmas, troubles or problems" that moral and rational reasoning becomes a social process, open for social analysis (Zigon 2007:140).

Interviewing participants, as Robbins (2004) observes, may stir a realisation of conflicting moral codes, ethics or questions of morality, providing a window in which they can see the contradictions with which they have to live. Questions of risks, rewards and motivation in clinical

trials may occur to both professionals and lay volunteers, but the way these risks are viewed will be different because the moral codes and cultural subgroups to which they belong may influence their perception of risks and shape their behaviour (Lupton 1999). Robbins's (2004) observation raises profound questions about the practice of semi-structured interviews in social research. Researching issues such as participation in clinical trials may prompt unwarranted rational responses (Callon and Rabeharisoa 2004; Will and Weiner 2014), particularly in encounters with strangers. I am aware that the interviews in this research took place in certain contexts and the analysis should take into account ways in which these contexts and certain questions may have elicited certain responses. Nevertheless, I take what was said in interviews seriously and do not intend to simply cast doubt on it as untrustworthy or accounts looking for approval.

3.7 Conducting ethical research

The research gained ethical approval from the University of Sussex social science research ethics board (see appendix four) before any advertisement or data collection commenced. Social research can involve an intrusion into people's private spaces; researchers must acknowledge the potential for exploitation of participants and try to avoid it. Ethical guidelines such as the BSA research code of ethics (BSA 2004) and those of the University of Sussex are intended to deal with such situations. In these codes special attention is drawn to researchers' responsibilities in ensuring participants are dealt with respect and their dignity is preserved; there is also a need for consent, trust and integrity in the conduct of research. These principles were essential in the context of my research. I made it clear to the participants that I was a researcher and offered e-mail contact details should they change their minds about being involved in the study. Information sheets (see appendix one) detailing what the study was about were provided to all participants. To ensure confidentiality, participants are referred to by a number prefaced by their role as corporate professionals, regulators or healthy volunteers. All consent forms were signed before the interviews began. Participants were assured of their rights to refuse to answer questions or discuss issues they were not comfortable with, to

withdraw from the interview at any time, and even to withdraw their responses after the interview. Data were stored in password protected files and backed up.

3.8 Trustworthiness – dealing with credibility and validity questions

The application of questions of reliability and validity to phenomenological research is always problematic (Bryman 2008). This is because qualitative research often takes as its focus of study the exploration and understanding of the subjective and contextual experiences of participants; it is not concerned with wider generalisation of findings to other contexts (Coffey and Atkinson 1996). However, this does not imply lack of rigour in qualitative research. What I set out to do was not to find the truth or "right" answers, but rather to use the available interactions with participants to identify critical aspects of their experiences and views and to develop plausible interpretations of their accounts. My aim was not so much to get it right as to get it "differently contoured and nuanced" (Richardson 1994, 521). An alternative to reliability and validity, as suggested by Lincoln and Guba (1986), is to consider the trustworthiness of qualitative research. The trustworthiness of my research had to be established in several stages: to start with, during the data collection and analysis phase the engagement with the participants was deliberately prolonged to establish trust and to become immersed in the data and the issues the participants were raising. The contact with participants did not end with the interview; besides exchanging e-mails to clarify issues after the interview I also held in-depth discussions with them about the research and their experiences as interviewees.

Trustworthiness was also established in the use of different sources of data; survey data, documentary analysis and interview data were combined, making the analytical claims from this study credible. Another means of ensuring trustworthiness was the peer debriefing in the form of feedback from my supervisors and colleagues (Lincoln and Guba 1986), who critically reviewed the work throughout the research process in supervisions and at seminars and conferences where I presented my

efforts. This ensured that the research process, analysis, difficulties and compromises in data collection, and ultimately the outcomes were subject to continuous interrogation.

During the research I shared some of my findings with participants who I chose for their interest in the research outcomes – what Woods (2006) refers to as "respondent validation". The aim was to make sure that I had accurately captured the participants' experiences, views, issues and feelings and put them across to others accordingly (Woods 1998; Denzin and Lincoln 2000; Woods 2006).

I developed a systematic audit trail of information, such as field, conference and supervision notes on which I based my actions and decisions. Systematic record keeping helps to give confidence in the findings of the research. In the next chapter I present a description and an analysis of the organisation and structure of regulation.

Chapter 4
Structure and Practice of Regulation

4.1 Introduction

Hochschild observes that some modes of operating in organisations supplant people's normal ways of acting with institutional mechanisms of conduct (Walker et al. 2012) in which individuals' actions are organised and shaped by institutional rules and customs (Hochschild 2003; Walker et al. 2012). In a typically hierarchical context, individuals are expected to work and act in keeping with standardised procedures. It can be argued that this is evident in the regulatory process of FIHCTs. As individuals assume their roles in this process, the institution they work for positions them in such a way that they view and respond to questions about institutions and their roles in a pre-defined and official way. This is clear from discussions about access to professionals as discussed in the previous chapter, where it was shown that professionals may be reluctant to express personal views on issues related to their work.

This chapter aims to answer the following research questions: how is the regulatory system of FIHCTs structured and organised in the UK? And how does the political, cultural, socio-economic, legislative and healthcare context in the UK shape the ways in which supranational EU regulations are interpreted and implemented by those administering, sponsoring and regulating the trials? In the first part of the chapter, I discuss the organisation and structure of regulation of FIHCTs in the UK. This section draws on data derived from analysis of regulatory documents. The second part uses interview data to explore how professionals view the regulatory system and the relationship between industry, regulation, the state, the market and the public. It discusses the fragmentation of the regulatory system by analysing two practices: payments to volunteers and volunteer registers. The chapter concludes by exploring how the interests of healthy volunteers are side-lined in a regulatory process that is driven by corporate interests and how this is symptomatic of the relationship between regulatory bodies, industry and professional interests in a market

economy.

PART I

4.2 Regulation

As outlined in the literature and context-setting section of this thesis, the pharmaceutical industry is more closely linked with global politics today than ever before in its history. There are profits and lucrative gains brought into economies of rich countries and even emerging economies such as India and Brazil by the pharmaceutical industry (Rajan 2006). In the following section, I outline how the regulation of FIHCTs is structured and organised at a global level by international agreements. A great deal of research into the regulation of the pharmaceutical industry has been carried out by Abraham and Lewis (2000) and Abraham and Davis (2012). This chapter builds on some of their observations to focus on the regulation of FIHCTs. I begin by describing the processes and structure of regulation using data derived from my own documentary analysis.

Existing regulatory structures – a fragmented regulatory system

As discussed in the literature review chapter, the regulations of FIHCTs can be traced back to the 1947 Nuremberg Code, which has been revised over time and given rise to many other guidelines such as the WHO 1993 Good Clinical Practice (GCP) guidelines. This was followed by the 1994 Council for International Organisations for Medical Sciences (CIOMS). Both agreements were aimed at improving the practice of medical research. In 1997 came the International Conference for the Harmonisation of Technical Requirements for registration of pharmaceuticals for human use (ICH). These were followed in the EU by the Clinical Trials Directive 2001/20/EC. Today in the UK the regulations of FIHCTs and other trials for medicines are governed by the Medicines for Human Use Act 2004 (amended). By 2011 the Act had been amended five times. In a broader sense, regulation of clinical trials is done at national and supra-national levels. Each government has signed up to international

protocols that prescribe how research should be conducted in their countries. The EU directive has instructions on the production, monitoring and administration of drugs. FIHCTs come under the production part of this directive.

The regulatory system can be summarised as follows: the UK regulation of clinical trials, FIHCTs specifically, is shaped by the EU directives on the conduct of clinical trials. At the apex of this structure is the European Council of Ministers. The council is responsible for setting overall policy direction on issues affecting all countries that cannot be resolved at micro-national levels. It sets EU priorities and gives political direction. With regard to clinical trials and other matters, the council often votes on the directives as part of the ratification process that decides if directives should be used at national levels; these define what is required before permits are given to market a product and conduct research in the EU. The regulatory approaches of the EU take varied forms, namely regulations, recommendations, proposals, directives and council decisions (Abraham and Lewis 2000) among others. A clear demonstration of the approach and attitude that regulators are expected to take when regulating clinical research is outlined in Directive 2001/83/EC which states that

> *"*(2) The essential aim of any rules governing the production, distribution and use of medicinal products must be to safeguard public health.
>
> (3) However, this objective must be attained by means which will not hinder the development of the pharmaceutical industry or trade in medicinal products within the Community" (European Commission 2001:1).

The directive explicitly states that disparities and variances in regulation in member states have impeded the market for medicinal products. These regulatory disparities are also thought to affect the EU internal market and the directives were aimed at removing these impediments (European Union Council 2001). Using Schutz's system of

relevance to explain the policy focus of the council shows that the motivational relevance – that which is of significance and worth acting on by the council – is the protection of the pharmaceutical market within the EU; this demonstrates how regulation, public interest and the market interact as issues of public safety and risk are taken as normal or secondary. By focusing on enhancing the market, the council showed where its interests lay. How this has shaped its response to issues such as payment to volunteers and safety, is discussed in a later section. Their position inevitably puts them on a collision course with public interests as these do not often tally with corporate interests.

The arm of the Commission responsible for medical and health policies is the European Medicines Agency (EMA), whose main functions are to protect and promote public health and animal health by appraising and supervising the use of medicines meant for human or animal use in all member countries. The agency is responsible for issuing marketing authorisations of drugs for use and sale in Europe in accordance with directives from the Council of Ministers. It is also responsible for monitoring safety of medicines (or pharmaco-vigilance, as it is termed in the literature) in the EU. The EMA also oversees the conduct of clinical research in member states. It provides guidance and issues directives on standards of practice. The agency is led by an executive director, with specialised divisions such as expert groups on human medicines, veterinary medicines and information technology and administration teams. These groups are in turn divided into small specialised groups (see appendix three for organisational chart). With regard to clinical trials, the EMA's Committee for Medicinal Products for Human Use (CHMP) is responsible for dealing with matters relating to medicines used in humans (EMA 2007). It issues guidelines on how medicines should be used and has the mandate to withdraw medicines deemed unsafe. The committee is comprised of members nominated by the regulatory bodies of each member state as well as Norway and Iceland (Vogel 1998). At a national level the EMA does not act directly on breaches of rules by industry; rather, such issues are addressed by the member states' regulatory bodies. However, countries are subject to directives issued by the Commission that

are then transposed into member states' law, which must be complied with. Of interest here is that the members of the committees are mostly people working in regulatory bodies in their member states. This suggests that practices at a national level are protected from independent scrutiny because those regulating at national level are also part of the team that issues directives on standards at the EU level.

The UK parliament may convert directives into acts or incorporate directives into existing legislation as part of the revision or compliance process. Within this framework the role of the state in regulation is seen as being the guardian of public health with respect to the conduct of clinical trials and the marketisation of pharmaceutical products for healthcare. In this role, issues of topical relevance (Schutz 1970) to the state are ensuring safety, equality and the welfare of those who, without positive action, may be excluded from benefits or even be exploited. The guardianship of the state includes supporting and maintaining an environment that facilitates the pursuit of research. This can put regulators in a difficult situation, as they have to ensure the safety of participants in research on one hand and facilitate the growth of the industry on the other (Nuffield Council of Bioethics 2011). Balancing public and industry interests can be awkward for regulators because industry is influential and powerful. While industry brings many benefits to the health of populations, pharmaceutical research is highly lucrative. This can raise issues of topical and motivational relevance (Schutz 1970), including public safety and the ethical conduct of clinical trials (Abraham and Lewis 2000). The task of ensuring compliance is assigned to the Department of Health (DoH), which works through the National Health Service (NHS), the Health Research Authority (HRA), the National Research Ethics Service (NRES) and national research ethics advisory panels (NREAPs) (HRA 2013). These are instituted in legislation. Among the roles of the NRES and NREAPs are to organise research ethics committees (RECs) and to oversee implementation of legislation. Their main responsibility is to ensure the ethical practice of medical and pharmaceutical research by safeguarding the rights, dignity and general wellbeing of research participants. Some RECs oversee reviews for clinical trials of investigational medicinal products (CTIMPs) involving healthy

volunteers (commonly referred to as type 2 RECs). Type 3 RECs review applications of CTIMPs but of phases other than phase I trials involving healthy volunteers. There are also site-specific review processes that consider the suitability of the principal investigators, investigate whether facilities are adequate and appropriate for the proposed trial and other issues such as prospective participants' insurance and healthcare (University of Brighton 2008 ethics guidance).

Alongside the RECs is the Medicines and Healthcare products Regulatory Agency (MHRA), an executive agency of the DoH responsible for regulating the safety, quality and efficacy of all medicines and medical devices. Within the MHRA there are several divisions but of interest to this research are the Licensing Division and the Inspection, Enforcement and Standards Division. The Licensing Division has four subdivisions which are in turn divided into four groups (see appendix three). It is responsible for ensuring the safety of medicinal products; its focus is on the composition of medical drugs, proposed dosages and routes of administrations. Of particular interest is the unit that is responsible for assessing applications for clinical trials; its focus is on the safety of the investigational medicinal products (IMPs) to be tested. Another subdivision of the MHRA, the inspectorate group, polices compliance with good clinical practice (GCP) guidelines. It inspects clinical trials units to check on the training of staff, emergency preparation and accommodation of volunteers, among other matters. Other organisations within this process represent the pharmaceutical industry. In the UK one such influential organisation is the ABPI, a government-recognised industry body representing research-based biopharmaceutical companies big and small. Their members are key producers of medicines used in the NHS. ABPI's main role is to lobby the government on issues of pricing and regulation (ABPI 2013). It also produces guidelines of good practice for its members; these are often endorsed by regulators and sometimes by the government. These guidelines are however not legally binding.

Other players in this process are NHS hospitals, with and without clinical research facilities (CRFs). NHS hospitals have several functions in

this system: acting as a source of patients for some early phase and almost always for later-phase trials and providing space and equipment for commercial research in some trials. Some CRO trial units are sited in or close to hospital premises. Alongside the CRFs are the CROs that specialise in organising and conducting clinical trials on behalf of pharmaceutical companies. The CRFs are publicly owned. They conduct mostly later-phase publicly funded clinical trials. They also lease their units to CROs which might need to use certain equipment and the specialised staff of the units. CRFs and CROs are at the frontline of clinical trials in the UK, though some pharmaceutical companies occasionally carry out research. Another category is charitable organisations, mostly disease-specific, that promote the interests of patients and research participants, such as Cancer Research UK and HIV and AIDS advocacy groups. A noteworthy omission is the lack of organisations that represent healthy volunteers. This is why healthy volunteers are often conflated with patients. The implication is that their needs – that is, of topical or motivational relevancy (Schutz 1970) – are thought to be the same as those of patients. But it is also a sign that they are seen as capable individuals, able to give rational consent and represent their interests. This will be discussed in more detail in the following chapter.

The structure of regulations in clinical trials is summarised in the flow chart on the next page:

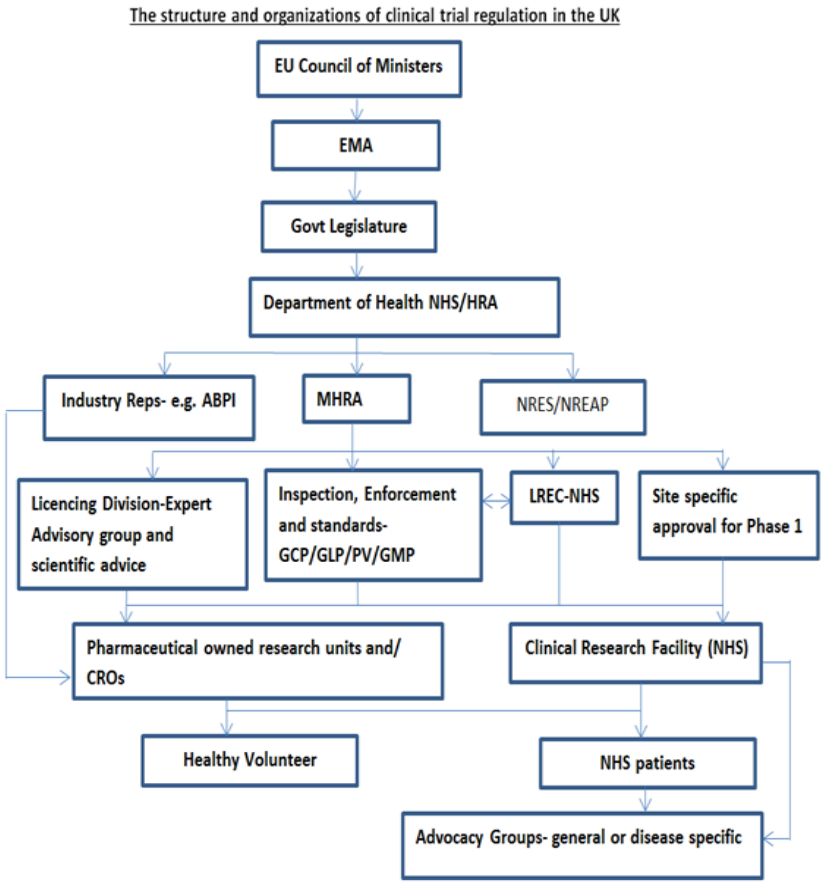

Figure 4.1: Structure of clinical trials regulatory system

The organisation and structure of the regulatory system is described and discussed in some detail to illustrate how complex it is and where gaps might develop within the system between international and national bodies, resulting in a fragmented system in which international regulations are not appropriately reflected in national legislation or are insufficient to address local/national issues. Even at a national level, regulatory bodies are disconnected from each other. Figure 4.1 portrays an orderly system of regulation. In practice, however, the regulation is not orderly and free-flowing; rather, it is complicated and fraught with political tensions and conflicting motivations (Schutz 1970) at almost all levels. Figure 4.1 does not clearly show the influence of member states and the industry on the regulatory process. As outlined in Chapter 2, member states have an interest in the regulation of the pharmaceutical industry as it is a major source of Western governments' tax revenue. The structure and

organisation of the regulatory process is more accurately shown in Figure 4.2 below.

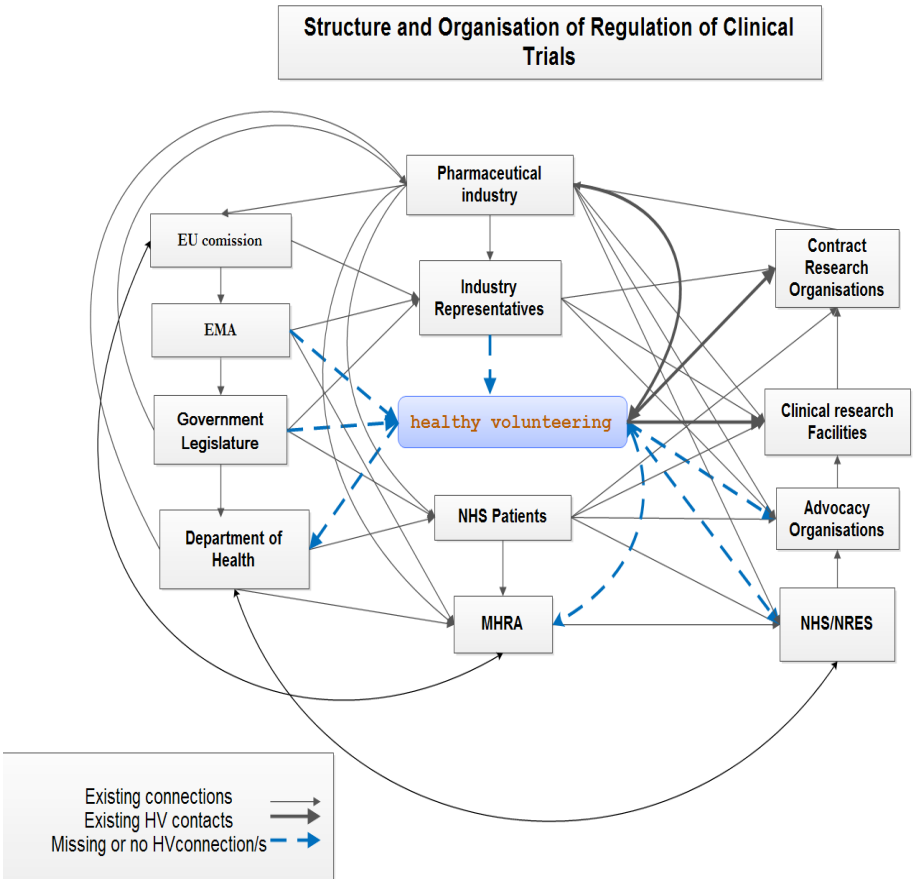

Figure 4.2: Convoluted Structure of clinical trials regulatory system

Another aspect of the regulatory process, discussed in the following section, is the relationship between science, uncertainty and professional work.

Science and uncertainty in the regulatory process

The practice of science should involve regular engagement with the issues that are of topical and motivational relevance to the public. Scientific and public interests are sometimes shared but at times they conflict. The public hopes for improved healthcare while the motivations of the commercial companies are to maximise profits; governments must attempt to strike a balance between the two. The drug development process is always imbued with uncertainties and shrouded in the politics of ethics.

The CHMP requires that the process of drug development follow strict procedures for safety testing. In determining whether a drug should

be administered to humans for the first time, regulators consult previous outcomes of the scientific testing of drugs in the production process. The process, discussed in Chapter 1, starts with testing of IMPs in animals, which must be done to an adequate standard, to ascertain toxicity and levels for human exposure. Once this is ascertained, FIHCTs (phase I) are carried out, in which the IMP is tested on healthy volunteers. Following phase I, if the IMP passes, are phases two and three in which the drug is tested on patients. The trials are done on small numbers of patients to test the effectiveness of the drug on the target health condition. After the drug is deemed suitable for human use, further tests and reports are required and further monitoring is done during the post-marketing licensing period referred to as pharmaco-vigilance. This process can be summarised in a figure 4.3 as illustrated by Abraham (1997: 157):

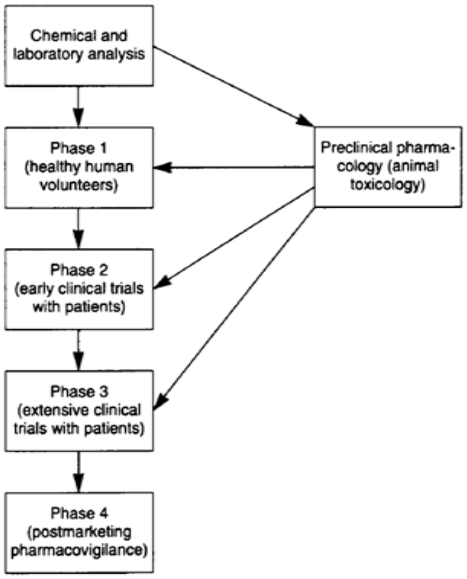

Figure 1 Drug development

Figure 4.3 Drug Development process: Adapted from Abraham, J. (1997), 6. The science and politics of medicines regulation. *Sociology of Health & Illness*, 19: 153–182

Of interest in this research is the uncertainty that surrounds the conduct of FIHCTs. As mentioned earlier, decisions on whether to test IMPs on humans depends on the nature of the tests in animals and the results. This involves identifying potential risk factors from the data (EMA 1998). For example, the mode of action of the IMP, including its nature

and intensity with regard to durability and reversibility of effects, would be carefully noted. Researchers might also consider whether a given compound and evidence from animal models regarding potential pharmacological toxicity pose risks for humans (EMA 2007). Further consideration is given to the nature of the target in the human body such as tissues and cells, and how this might vary between individuals. Moreover, researchers may query the relevance of applying the animal model to humans in terms of its "homology, signal transduction pathways and the nature of the pharmacological effects" (EMA 2007:5). There must also be assurances that reliable methods will be used in determining the starting dose in humans and the formulation in which it will be administered, as there are risks of overestimating the starting dose. In summary, the studies involve testing of drugs "in vivo" (in living whole animals) and "in vitro" (in cells in petri dishes in the laboratory) (EMA 1988: 2007) with a view to ascertaining the toxicity of compounds for humans. These studies provide the basis for decisions for regulators as to whether a study should be carried out in humans. While the pharmaceutical industry organises the clinical testing, tests for toxicity often involve the wider scientific community, from which experts, mostly the licensing team at the MHRA, give their opinion as to whether formulations can be safely tested on humans. In general, in FIHCTs and other phase trials, testing of drugs takes the form of double-blind trials to ascertain the actual effects on the drug in humans (EMA 1998).

This summary of how safety concerns are addressed in the drug testing process illustrates possible areas of uncertainty in FIHCTs. It has become clear that animal testing is not always a reliable indicator of how human subjects would react to compounds (Litchfield 1961; Posvar and Sedman 1989), as the 2006 Northwick Park incident and others attest (Hanke 2006; A. Hedgecoe 2013). Differences in animal and human physiology and biology mean that some drugs might not work as expected in humans and trials sometimes do go wrong. This is something that the regulators rightly acknowledge:

> Qualitative and quantitative differences may exist in biological responses in animals compared to humans. For example, there might be differences in affinity for molecular targets, tissue distribution of the molecular target, cellular consequences of target binding, cellular regulatory mechanisms, metabolic pathways, or compensatory responses to an initial physiological perturbation. (European Medicines Agency EMA CHMP expert group 2007:6)

Some animal studies with highly species-specific medicinal products may not produce the expected effects in humans and may also result in incorrect predictions of pharmacokinetic and pharmaco-dynamic outcomes (EMA CHMP Expert Group 1988). The process of transitioning drug testing from animals to humans is complex since it is difficult to ascertain risks to humans (EMA 2009; EMA 2007). It makes FIHCTs very risky, too. However, the regulators are often quick to argue that this does not necessarily mean that FIHCTs have increased risks. Their arguments are often based on the views of teams of scientific experts involved in the process. It is their reports, reviews and assessment from this process of drug development that regulators use to make decisions about licensing or issuing of permits to conduct clinical trials (Abraham 1997). However, other issues relate to the potential to extrapolate studies in animals – for instance, the fact that only a small portion of the human population is given the IMP – means that the outcomes from such studies cannot be extrapolated to the wider population. In addition, although volunteers are examined before being admitted to the trial, people's states of health differ according to their age, weight and other factors, and they may thus respond differently to drugs during and after clinical trials. Obviously, there is the argument that tests are done to check for toxicity during the post-marketing phase of drugs testing (Abraham 1997). However, as Litchfield (1961) and more recently Posvar and Sedman (1989) and Abraham and Davis (2007) find, the outcomes of toxicity testing in clinical trials cannot be relied upon to produce consistent results. Even today these issues are still cause for concern, as can be seen in the discussion among global experts on drug discovery and the results from animal testing as a

basis for human trials (Clotworthy 2012). In addition, there may be different scientific criteria applied to how these three sources of data – the pre-clinical, clinical and post-marketing – may be interpreted (Abraham 2007). This adds to the uncertainty in these processes.

In summary, it is crucial to appreciate the interaction of science and politics of regulation in this process; these uncertainties do not occur in a vacuum. The entire process is imbued with competing and sometimes conflicting motivations. Pharmaceutical companies may want a fast-track process to approve drugs in order to maximise profits; governments are the custodians of public health but see the pharmaceutical companies as sources of economic growth. Then there are patient groups and individuals who may demand access to new and better treatments but are also wary of health risks. These interests may conflict, but they are not exclusive.

The above discussion and the data derived from documentary analysis in the chapter so far have revealed the multiplicity of actors and processes involved in both the regulation and the business of clinical trials. Regulation is responsible not only for ensuring fairness from a social justice perspective but also for defining, positioning and legitimising forms of agency. As Zhao (2005) observes about the role of classifications, regulation institutes, authorises and legitimises the practice of clinical trials. Regulation assigns different actors roles and responsibilities and defines who is responsible for what and thus contours issues that are relevant to them (Schutz 1970). Through regulation the discourse of bioethics, which is associated with autonomy, informed consent and volunteering, has become a central part of clinical trial governance. This discourse creates boundaries by defining how far ethics committees or licensing teams can go in their operations, as clearly illustrated in the quotes from Directive 2001/83/EC (cited in this section, above). In doing so, regulation represents political power that is used to define and create boundaries (Zhao 2005). Thus, regulation needs to address questions such as how the pharmaceutical industry, as a dominant force in the business of clinical trials, influences the roles of different players and the terms on which they are dealt with. It is also important to note how uncertainty is part of the

clinical trial process. Though experts are involved throughout the clinical trial processes, there are no assurances that outcomes of trials will be of benefit or relevance (Schutz 1970) to the public. Nor can guarantees be given about the outcome of clinical trials involving healthy volunteers. Having set out these organisational complexities, in the following section I focus on professional views of the clinical trial regulatory process.

PART II

4.3 Professional views on the regulation of first-in-human clinical trials

I refer to participants in this research who work for CROs as corporate professionals and those working for regulatory bodies as regulatory officials. Part I discussed the structural organisation of the regulatory process, based on documentary data. Drawing on data from interviews conducted for this research, I now discuss how professionals in the field of clinical trials view the existing regulatory process. Having reviewed the structure and organisation of the regulatory process, it is important to provide a critical analysis of the views and experiences of professionals and healthy volunteers in regard to the adequacy of the process, to show how the regulatory system operates in practice. Professionals in the pharmaceutical industry and regulatory bodies were interviewed in two groups. Those in the industry tended to believe that regulatory frameworks were more than adequate. They often expressed a fear that anything more would constitute over-regulation, which might drive business away:

> initially I think everyone was apprehensive about the new requirements that were put in place in 2004. There was a general view that it's too much regulation (Corporate Professional 1).

> I think the process is brilliant now and I am satisfied with the requirements, though somehow some of the things border on over-regulation and could put business off (Corporate Professional 2).

These concerns and attitudes were echoed by an official with a regulatory body who talked about the response of the industry to the changes in the clinical trial approval systems in 2004, when the government introduced compulsory submissions to the MHRA and to ethics committees for FIHCTs:

> concerns from industry when we started this in 2004 were on how much that affected their business … in terms of how fast the turnaround of applications would be and whether it would slow down the process for them (Regulatory Official 5).

Issues that were of topical and motivational relevance (Schutz 1970) to professionals from the industry were mostly that the regulatory process could make it difficult to conduct their business. This has always been the response by industry to regulation and shapes the interactions between corporations and regulators. Abraham and Lewis (2000) observe that the industry's interactions with governments and regulatory bodies are aimed at reducing time and costs and influencing the regulatory process. Some professionals felt that regulations were not excessive but were useful in bringing about confidence and trust in the industry, supporting the idea that it is safe to do business in the UK. One participant said incidents of trials going wrong – such as the Northwick Park incident and the death of a healthy volunteer in the US in 2000 from hexamethonium, a drug previously used in the 1950s and 1960s to treat high blood pressure (Savulescu 2002) – made people question the clinical trial process:

> having said that [that regulation could impede business] … for me the feeling is that the process this brings about changes, and much needed changes, which I think restores public trust … in the industry, on the other hand (Corporate Professional 1).

Fragmented regulatory system

For those involved in the regulation of the industry, there was a common feeling that while the framework was effective, there was room

for improvement. A regulatory official who has served on ethics committees said:

> [The] MHRA has been good in that they have raised awareness in areas where people thought they were doing fine but who probably would not understand that the rules and regulation applied to them … Shall we go back to unregulated clinical research? I don't see why we should. Now I am not saying the system is excellent. We could do better but things are now better than before (Regulatory Official REC 11).

> Of course the system is better than before. There are things that need improving and we are heading in the right direction (Regulatory Official 9).

The participants talked of regulation being better now than the system that was in place prior to 2004. By this, the participants' were referring to how the existing process provided what they considered to be a systematic process of accountability compared to the previous system where little if not no review of FIHCT applications was done by regulators. In the previous system as outlined in Chapter 1 of this thesis, investigators conducting FIHCTs were not required to submit their clinical trial applications for review; instead these were often reviewed internally. The introduction of the 2004 medicines for human use regulation, outlined in the regulatory context in chapter one of this thesis, required that all clinical trials including FIHCTs be subject to systematic regulatory review. One official, while welcoming the improvements, was critical of the way the existing system works:

> I think the problem with the existing system, good as it may be, is that there is a lot of lack of clarity on who does what. For example, the Northwick Park incident highlighted, in my opinion, that there was this assumption that everyone gives peer review to everyone and there was no flow of information to others. Obviously things are improving but we can do better (Regulatory Official REC 10).

This reference to the 2006 Northwick Park incident illustrates how the regulatory process operated on an assumption that everyone was checking what others were doing but without clearly defined roles and responsibilities. The fault is seen to lie with the system of regulation and

not with individuals or institutions. The above quote also illustrates the disconnected nature of the regulatory process – what I call the "fragmented regulatory system". While some parts of the process are clearly defined, other aspects are not well integrated, leaving gaps that can be exploited by industry. Some argue that some elements of the process are conveniently left out of the regulatory process in the interest of the industry (Abraham and Lewis 2000; Davis and Abraham 2011; Davis and Abraham 2013). In other words, it is of topical and motivational relevance to both regulators and the industry (Schutz 1970; McGoey 2012). An example is the lack of clarity regarding payments to volunteers, which works in the industry's favour.

Staff involved in assessing applications and inspection of clinical trial units felt that the system had generally improved and would continue to improve:

> Obviously things are better now but we can do better. But overall I am satisfied with the way things are going in regulation and there has been improvement in practice in many areas (Professional 6).

Participants responding to questions about the adequacy of regulatory frameworks tended to take an official line. Getting them to express their opinion on the subject was challenging:

> Mwale: How satisfactory is the regulatory system today, in your opinion?
>
> P: Well, what do you mean? Um, it is good. I'm happy, I can say it's not bad at all and I think we do a good job. That's why we are here. If you ask everyone here they will tell you the same. You are not going to quote me, are you?
>
> Mwale: Well, I might.

> P: Well, I think the system works well. Might need to be improved in some areas but it's working well (Regulatory Official 8).

> I don't think I want to answer questions about the shortfalls of the existing system, because I think that the regulation of first in-human studies is very good and, um, you could not possibly put any more into the current review process to make it any safer or to make it … um … I think it's very robust as it stands. I don't think anything else that you can put in would make it more robust (Regulatory Official REC 10).

The last quote was the initial response to the question about the adequacy of the regulatory system. This shows how much the professionals tried to avoid questions about the regulatory process. To answer these questions, they required a great deal of probing.

Some participants spoke of the challenge of making EU directives work in practice. EU directives were often thought to be inadequate – hence the need for supplementary guidelines for practitioners on the frontline:

> Oftentimes the EU directives are not sufficient or may not be clear or relevant to staff in units so we have to make additional guidelines to help people put in practice EU guidelines … In some cases we used to find that what was for us an obvious thing for practice, such as making sure that each unit has an easy access area for ambulances clearly marked out, was not in place, or having a crash trolley always ready and restocked (Regulatory Official 8).

This comment indicates the challenges of international regulation while strengthening the case for a contextualised regulatory approach. Varying socio-economic conditions and cultural circumstances make the application of the harmonisation principles problematic; member countries have different problems and in some cases different cultures of working, which makes some of the directives difficult to apply (Abraham and Lewis

2000).

Participants generally felt that the system was adequate in dealing with regulatory issues, but there was some apprehension about regulatory frameworks, and some concern that too much regulation could slow down the approval of applications and increase costs. It was also acknowledged that the guidelines and regulations in place were not adequate and some participants believed that certain issues could not be regulated. There was also a feeling that the EU directives are not always clear and needed to be supplemented by local in-house instructions.

The following section focuses on aspects of regulation in the UK which are of particular concern for this thesis: payments and prevention of over-volunteering.

4.4 Regulating monetary rewards to volunteers

Although there are concerns about the potential for exploitation when rewards are offered in clinical trials, there are no clear guidelines about how much volunteers should be paid. The bioethical discourse about payments to volunteers regards them as compensation for their time and inconvenience, not as wages (Abadie 2010; Geissler 2011; Cooper and Waldby 2014); healthy volunteers are considered capable participants who are able to represent their own interests. Opponents of this view argue that inequality in society predisposes some people to take part in clinical trials because of their straitened financial circumstances (Lemmens and Elliott 1999b); hence the need for guidance and protection for vulnerable groups. While legislation in the UK acknowledges the possibility of exploitation, it does not provide explicit guidance on how much volunteers in FIHCTs should be paid. The issue is mentioned only as a matter that RECs have to take into account:

> (5) In preparing its opinion, the committee shall consider, in particular, the following matters –
>
> (a) the relevance of the clinical trial and its design;

> (b) whether the evaluation of the anticipated benefits and risks as required under paragraph 2 of Part 2 of Schedule 1 is satisfactory and whether the conclusions are justified; ….
>
> (f) the quality of the facilities for the trial;
>
> (g) the adequacy and completeness of the written information to be given, and the procedure to be followed, for the purpose of obtaining informed consent to the subjects' participation in the trial; ….
>
> (k) the amounts, and, where appropriate, the arrangements, for rewarding or compensating investigators and subjects; (Medicines for Human Use Act 2004 part 3, 15 (5).

Among professionals working on ethics committees, accounts of lack of clarity were common. One noted:

> There is no guidance, rules or regulations about how much people should be paid for taking part in clinical trials. The only arbiters of it are the ethics committee because you have to tell an ethics committee how much compensation you are going to give in a study and they consider that to be an inducement and hence an ethical issue. But then how [to] come to that decision is not laid out in any detail. It is possible that … there … is … some variance in the way that different ethics committees decide on the same issues. Whether state involvement would make it any better I doubt (REC Official 11).
>
> No, there are no legal or set guidelines on how much volunteers have to be paid so it is hard I think for researchers to know. Most researchers go based on what they can get in a grant, for example, they have been awarded, but that is for academic trials. For commercial ones it is at their discretion to determine and we just have to ask how they arrived at the fee (REC Official 9).

It is noteworthy that while for industry the issue of payment is seen

as compensation, ethics committee members in particular talked of payments as inducement. The difference shows how industry tries to downplay the implications of payment, while ethics committee members were acutely aware of the problems that payments to volunteers give rise to in clinical trials. The lack of clarity on guidance is felt at national and international levels (Lemmens and Elliott 1999). The quotes above show that ethics committees hold different views about what reasonable payment means which means variable practices (Petryna 2009) among ethics committees. This is indicative of the differences in topical and motivational relevances among professionals, industry, regulators and the public. The only clear view on payment comes from the ABPI, which in its 2012 guidelines (and previous versions for clinical trials) states that:

> So it is right to pay subjects – healthy subjects and patients – who volunteer for Phase I trials more than just any expenses that they incur. The amount should be related to the duration of residence on the unit, the number and length of visits, lifestyle restrictions, and the type and extent of the inconvenience and discomfort involved. As a guide, payments should be based on the minimum hourly wage … and should be increased for procedures requiring extra care on the part of the subject or involving more discomfort. Payment must never be related to risk (ABPI 2012:20).

The first part of this statement arguably disqualifies the second part relating to risk because once payment is linked to discomfort, it is likely to increase. That "discomfort" and the link to risk occur in the same guideline also raises questions. Does "discomfort" mean only needle pricks and the frequency with which the subjects give blood, or does it include side effects? If it includes side effects, is risk a consideration? The dearth of comprehensive guidelines on payment to volunteers is paradoxical because it is generally agreed by academics and regulators, among others, that healthy volunteers are predominantly motivated by the payments on offer, and yet it is contended that the rewards should not be the primary motivation (Schutz 1970; Lemmens and Elliot 1999; (McNeill 1997; Macklin 1989). By contrast, the focus in medical and pharmaceutical

discourse positions healthy volunteering as an act of altruism. The tendency to avoid discussions and to provide clear guidelines about monetary rewards is widespread. In the Northwick Park incident, for instance, payments are said to have played a major part in recruiting participants who could not resist the proffered rewards (Spielman 2007), but the ensuing investigations and reports of the MHRA and the DoH did not raise the issue of monetary rewards. The concerns were mainly about safety in the development, transportation, administration and monitoring of the test drugs and subjects (MHRA 2006, DoH 2006). The only guide to payment, that given by the ABPI, is not legally binding or a practice which CROs are obliged to observe. This was confirmed by one of the professionals:

> The guidelines are not regulation; they are recommended best practice and also serve to signpost the reader to the relevant regulations – you can clearly see these listed in the appendix. Regulation is set by the medicines regulators – MHRA, and EMA. The regulators are independent of ABPI (Corporate Professional 4).

UK legislation does not cover issues of payment to volunteer participants in research. Rewards to volunteers are mentioned in the 2011 Nuffield Report on organ donations, which supports the idea of payment to volunteers and alludes to the need to ensure that payments are appropriate. It also regards payment as a form of benefit for volunteers, as in the gift relationship, discussed in Chapter 2, between the researchers, research and participants (Nuffield Council Report 2011). The view is that researchers and participants both benefit. The concept of payments given in the Nuffield Report and discussed among professionals is influenced by the Belmont Report (1979), which construes payments as benefits to research subjects. Though not a legal document, it has influenced policies and guidelines on ethics widely among research participants. Like many regulatory instruments, the Belmont Report emphasises the assurance of informed consent and the avoidance of exploitation of research subjects. Legitimate as these concerns are, however, there are conflicting

assumptions. Construing payments to volunteers as benefits represents monetary rewards in clinical trials as virtuous, and so obscures the inequality and risks that certain groups of participants encounter (Lemmens and Elliott 1999; Geissler 2011). As shown in Chapter 2, the concept of informed consent sees individuals as autonomous beings in a market economy who are at liberty to accept money to put their bodies at risk. But if individual liberty is worth upholding, in this case it is at odds with the principle that individuals should be protected from exploitation and harm (Lemmens and Elliott 2001; Jonsen 1989). This observation emerged in my research; several corporate professionals and regulatory officials felt that payments were problematic in clinical trials, as the following quotations showed:

> Yes, I think payments do affect and may actually coerce volunteers into participating … Yes, I think that's always a concern, I do think that is exactly what happens (Corporate Professional 2).

> Of course in any culture that pays people to take part in studies there is always this debate as to whether they take part for the money or they are taking part in research because they have a greater understanding of things like research processes. So obviously, when you start paying people thousands of pounds to take part in research, then you really have to think of that. Is this more of an inducement rather than that they are taking part for compensations, and people have to think, is it about that? (Regulatory Official REC 11).

There were different views about what should be done to address the problem. REC members generally saw the need for corporate professionals, academics and regulators to discuss the issue. For one such official the problem was that issues of payment are often not of topical relevance among professionals in the field:

> I think it's something that we should be talking about in the research community much more than we do. We don't talk very much about issues of compensation, we

> often teach [people] we are teaching about research that any compensation must be seen to be appropriate and not too excessive. But we rarely talk about or ever put figures on it and perhaps we need to as a unit, as professional groups, as multi-disciplinary professionals. We need to discuss what is appropriate and what is too much. Where is the line crossed? (Regulatory Official REC 11).

The discussion on payment would ideally influence not only legislation but also best practices of dealing with payments and the recruitment of volunteers.

No-man's-land of regulation

Corporate professionals and regulators in this research were generally resigned to the anomalies in the issue of payment. They all saw the problem of payments as inevitable, something they had nothing to do with and could do nothing about; in other words, payments were not of topical and motivational relevance. As one remarked:

> Oh, yes, payments and coercion do concern me … but I have had to live with it and … I don't think there is anything I can do about it. What can you do? I mean, you can't bar poor people from taking part because that's discriminating against poor people. You can't pay rich people more than you pay poor people because that would seem even more unfair on the poor people. Erm, so we pay everybody the same and that means it is more of an incentive for poor people, which is a fact. So … yes, it's always been our … my concern but it's not one that I certainly know the answer [to] … and I don't think they [ethics committees] know the answer either, so it's just a difficult question we have to live with (Corporate Professional 2).

> If we stop paying them, who will want to take part in a clinical trial as a volunteer? It would be easy for me to say here, let's stop paying people for volunteering, but if we don't pay people, we may not have studies because no one will volunteer (Regulatory Official REC 11).

Such comments show how issues that directly affect volunteers seem to be of little significance to regulators. They also show how regulation limits and defines roles of participants and how free market considerations permeate the regulatory process. Payments to volunteers seem to present a dilemma to the professionals running and regulating clinical trials. They all felt that whatever changes they brought about would disadvantage participants one way or another. Members of ethics committees can do nothing about the problem because research has to take place regardless. Regulatory officials with the MHRA and corporate professionals with the ABPI avoided talking about payments, referring such questions to ethics committees:

> Well, interesting question about payment but I can't say anything about that because we do not deal with payments to volunteers. The best people to answer those kind of questions are the ethics committees (Regulatory Official 6).

> The questions you pose [about the payments] are ethical questions, best answered by the National Research Ethics Service. We have nothing to do with that and so I will not be answering those questions (Regulatory Official 8).

Professionals generally regarded payments as a "street level" problem or as something they would consider at some unspecified point in time. There was also a tendency to "pass the buck", as shown in the foregoing extracts, and a suggestion that ethics was the remit of a specific group. Ethics committee members felt that it was not their role to deal with payment issues. Payments are obviously of different topical and motivational relevance to the different professional groups represented in this research. In the following extract, the rationale for disregarding the issue was compliance with anti-competitiveness rules:

> These guidelines are not legally binding and they are not obliged to follow these – they are just guidelines highlighting best practice. We can't prescribe what they

> should do because we do not want to breach anti-competiveness rules (Corporate Professional 4).

By invoking anti-competition rules, the interviewee clearly situated healthy volunteering in the market economy; any attempt to define or restrict payments to volunteers is seen as interfering with the market. Meanwhile, ethics committee members, although they recognised that they have the authority to ask questions about payment, talked of feeling powerless to deal with issues of payment because of restrictions on what they were allowed to ask. Some of them felt that the problem with regulating payments was that money meant different things to different people, which demonstrates how topical and motivational relevances can be imposed by wider institutional factors:

> Money has different significance to people who are in different life situations. So if you are struggling financially … there is more of an inducement to some people than others. So the studies are better value for some people, there is greater incentive. The money is a bigger incentive to people who are poor. And so if you are unemployed you … would value the payments that [are given] much more highly than … a well-paid person. And I … don't think there is any way around that (Regulatory Official REC 11).

What this means is that payments to volunteers are shifted into the margins or what I call the "no-man's-land" of regulation, resulting in varied practices and placing financially vulnerable individuals at risk of coercion and exploitation (Petryna 2009). Corporate professionals on the frontline mostly believed the problem of coercion had less to do with the inducement of higher payments than with how ethics committees failed to see the payments as coercive most of the time:

> …but I don't think it actually happens because the ethics committees are very worried about coercion … but if anything, ethics committees encourage us to pay more. We very rarely, if ever, have been asked to reduce a payment – if anything the reverse. Ethics committees

> don't seem to see the coercion risk. I don't think it's coercion, I think, as I mentioned just now, the volunteers, if anything, think that if it's big payments then they think it [the clinical trial] must be dangerous, but it's not (Corporate Professional 1).

For corporate professionals generally it was the healthy volunteers' views of payment that seem to be of relevance. What was of topical relevance was that healthy volunteers interpreted being paid more for their involvement in a clinical trial as an indication that the study was high-risk. The focus was on protecting the image of clinical trials; that way they might be inclined to pay slightly less:

> So they say things like they know there are risks and some of them think they get, genuinely get, more money because it's risky. And of course, all those things are not the case, erm, because you don't get more money because it's risky. In fact they are remarkably safe but the volunteers don't necessarily think they are … if we were giving them danger money we wouldn't be, erm … erm, that means that the study isn't safe and so we wouldn't be doing it. But, erm … many of the volunteers don't really see that; they think that these things; they don't realise perhaps that the studies are as safe as they really are (Corporate Professional 2).

They argued their payments bore no relation to the risks involved but rather depended on the length of time spent in the trial. That risk is a consideration for volunteers was confirmed by one REC official:

> People tend to factor in additional payment such as [for] discomfort and time. For instance, if you are spending 24 hours in a unit and you are having loads of blood samples taken [or if you had] a bronchoscopy, just for argument's sake, then is it right that you get paid the same amount of hours in the unit as when you give two blood samples [on a short visit]? Then I would say no because actually they have got the pain and discomfort of all of the procedures and risk associated with the

> procedures. So the risk is greater. Therefore, we should recognise that risk (Regulatory Official REC 10).

When asked how payment for clinical trials was calculated, a regulatory official replied:

> …you might say this is not minimum wage work. You are exposing yourself to more risk. People would argue you need to be paid more for that. This is not just like stocking shelves in Tesco's; this is more. There is potential for a problem here. You have calculated those risks and you are making an investment in it. So I could see the argument for that (Regulatory Official REC 11).

In interviews, professionals were asked to considered ways in which additional procedures – linked in the ABPI guidelines to "discomfort" – conferred risk. CROs and pharmaceutical companies would rather not admit that the trial payments were linked to risks because they would want to be seen to be protecting volunteers from risk; besides, it would discourage people from taking part in clinical trials.

This section has highlighted the differences between written guidelines and what participants in the study say about the situation regarding risk and payments. In addition the discussion has highlighted how certain views about payments to volunteers permeate the regulatory process of FIHCTs to those feeling they have little influence on how this should be changed are clearly reflected in the accounts cited above. The difficulty of ensuring public safety on one hand and creating a climate in which industry can flourish on the other can clearly be seen in these accounts. In the process, issues of public safety are shifted to the "no-man's-land" of regulation as industry interests take priority.

The following section looks most closely at the fragmented nature of the regulatory system and at measures to stop over-volunteering.

4.5 Safety: the role of volunteer registers

Another issue that is often shifted to the "no-man's-land" of regulation is that of monitoring and reducing over-volunteering. Due to

the amount of money on offer in clinical trials, there are concerns that some healthy volunteers may be enrolling in a succession of clinical trials without a safe interval. Abadie (2010) talks of "career volunteers" in clinical trials. The phenomenon is of motivational relevance to regulators and researchers alike because there may be some drug interactions that affect findings and thus trial outcomes. It also poses a danger to the health of the individuals if there is a drug interaction or if they donate too much blood. In any case, legislation requires researchers to demonstrate that they are checking on the health of the research participants:

> (h) arrangements for the recruitment of subjects, including the materials to be used;
>
> (i) the criteria for inclusion and exclusion of patients, including justification for recruiting from vulnerable groups;
>
> (j) in the case of Phase I trials, methods for recording and verifying health status for healthy volunteers;
>
> (k) procedures for checking simultaneous or recent involvement of potential subjects in other trials … (Medicines for Human Use Act 2004; schedule 3, part 1 (1).

The requirements do not specify how this should be done. Nonetheless, in response the industry has reluctantly devised a system of how to address them – healthy volunteer registers. As one professional noted:

> Some things we have done like the over-volunteering strategies … the MHRA was making threatening noises about things and we have had to do something about those things (Corporate Professional 2).

The healthy volunteer registers are intended to function as a database that CROs use to screen recruited participants prior to admission.

A passport number or other suitable identifier is used to check if the individual has been on a clinical trial within, say, the last six months. In Europe, the best-regarded register is one used in France, the Fichier National/Volontaires Recherches Biomediclaes (VRB). It is a single national register used for all research run by CROs there. By contrast, in the UK there are multiple registers kept by different CROs and no coordination between them. Other measures are the "over-volunteering prevention system" (TOPS) and the National Volunteer Register (NVR), which maintains data to a certain national level and is rarely used, and the Volunteer Inclusion Period (VIP) register, which is available for use in Belgium, the Netherlands and Germany, but at a fee. Some CROs access the VRB to check on international volunteers. Such databases store information such as age, gender and passport numbers and check for recent involvement in clinical trials. They are organised and managed by individual CROs. Regulators do not regard the registers as part of their remit; rather they emphasise that something is being done demonstrably to avoid over-volunteering:

> We do not see how this register works. I mean, we do not regulate the register. Obviously, what is of interest to us is that they are doing something to mitigate against overuse of volunteering (Regulatory Official REC 8).

Asked if there were concerns that the registers might fall short of their intended purpose, the official responded:

> Well, we are aware that it's not 100%. You know, if people want to beat the system they can actually do it … but at least it's there.

There was no consensus among professionals in the field with regard to the effectiveness of registers or which was best suited to dealing with over-volunteering. That is borne out by the fact that there are multiple registers. Proponents of TOPS argued that their system was effective and had reduced the problem of over-volunteering. This group of participants had analysed data over a period of four years and they were

able to identify about one percent of the 7,000 people they had checked in that period as having come from another trial within the previous two to six weeks:

> We knew it was working because the rate at which we detected over-volunteering has since been going down (Corporate Professional 2).

However, proponents of the NVR argued that TOPS did not work and was not best suited to detecting over-volunteering because using passport or national insurance numbers was always suspect. They argued that the system allowed for multiple registrations, and the argument that detection rates had declined could be seen to be a result of people finding ways round the system to avoid detection. The other issue that causes conflict is the organisation of the programme itself. Registers maintained by individual CROs might give competitors access to their contact lists of volunteers, which has prompted the development of alternative registers. For proponents of NVR, the database approach to monitoring over-volunteering was not ideal. Instead, they favoured a search engine system in which details would not be shared but show the result of a search indicating whether a volunteer was suitable for trial:

> The whole TOPS business is not ideal at all. I think we need an independent system, not one run by your rivals, because I wouldn't want to share the details of my volunteers with my competitors. We need a search engine system and not a database where all details are revealed. You just want an indication, is this person suitable (Corporate Professional 1).

It is clear that there are tensions and discontent over the use of volunteer registers. The implications for safety are that people can go through the system undetected. For instance, if they have been tested in a unit using a different system, their details would not show in a subsequent trial unless data from all units were synchronised into one register. The problems with volunteer registers are heightened by the differences in

views about the topical or motivational relevance of registers among professionals, both those in regulation and those running clinical trials. This highlights an important issue about competition in the industry. The registers are problematic because they are sponsored by pharmaceutical contract research companies who do not want to share the details of volunteers with competitors. For regulators generally, over-volunteering was not of great concern in the UK. It was, however, seen to be a problem in the US:

> I think there probably are people like that but I think it is less of a problem in this country than it is in other countries like the US, where the culture of paying people to do research is embedded in their way of life (Corporate Professional 2).

There was also an implicit view that there was little need to address over-volunteering in the UK:

> Nobody really wanted to do it, because they didn't think there was a problem [with over-volunteering] and they did not want the … one extra thing…[which is] to check in TOPS. Yet it's very easy but it's still an extra thing, so they didn't do it (Professional 2).

There are others who believed that over-volunteering should be taken seriously. They cited the fact that people can cross borders in Europe and enter the UK to take part in clinical trials at any time.

> Most people in industry do not think this is a problem but I have seen with my own eyes we have a lot of people that cross borders to take part in clinical trials and this presents a challenge for us but also even local people who overdo the trials (Corporate Professional 1).

These participants saw a need to bring about an EU-wide register to deal with cross-border over-volunteering; failure would compromise efforts in the UK to prevent people from enrolling in multiple trials:

> … because if you do not address this [volunteers from across the EU] it is self-defeating. If you get people that have just been in a trial coming to you and you have no mechanism to check for that except their word, which may not always be accurate … but I also understand the challenges that are there to bring such a register into place (Regulatory Official REC 10).

The lack of regulatory clarity on this issue is linked to the neoliberal view, discussed in a previous section, of individuals as rational actors who are free and capable of making rational decisions and to resistance to restricting volunteer involvement. At the time of writing, regulators had responded to the idea of being involved in volunteer registers. The Health Research Authority (HRA) has taken over the running TOPS (HRA 2013). The impact of this change remains to be seen, and the idea of an EU-wide register remains unaddressed.

The use of registers and greater state involvement in issues of payment to volunteers conflict with the ideals of the free market. Lack of state involvement in the regulation of these issues means the state is not seen to be actively infringing on individual liberties (Sayed et al. 2014). While the professional view of clinical trials regulation is focused on process and systems, there is a need to consider how these work in practice and how they affect healthy volunteers (Hochschild 2003).

This section has shown how the regulatory system runs largely on self-regulation. It is clear that CROs and CRFs are expected to put in place measures to prevent over-volunteering, such as volunteer registers, but the measures are not clearly defined. Clinical trial units and pharmaceutical companies are expected to devise their own systems, which are subsequently accepted by the regulators. This is one example of how science and politics collaborate to create self-regulation. Regulators allow industry some freedom to determine how they will be regulated, highlighting another shortcoming in the regulatory regime.

4.7 Summary

This chapter has illustrated the relationship between the state,

industry (the market) and healthy volunteers. It has shown that the organised and seamless regulatory process portrayed to the public is actually a complex activity fraught with conflicting interests and shortcomings. Uncertainty in the science of clinical trials is equally a part of this process and adds to its complexity. The chapter critically examined the concept of healthy volunteers, commonly held throughout the regulatory system, as rational actors capable of advancing their interests in market-oriented clinical trials. However, such tendencies contribute to a "fragmented" regulatory system, and the responsibility for protecting healthy volunteers in clinical trials is often left in a "no man's land" of clinical trial regulation. The research found that some issues that might be expected to be regulated and overseen were left to the industry to deal with, resulting in a lack of clear guidelines on payments for volunteers and the inadequacies of volunteer registers. This allows industry the freedom to deal with volunteers on their own terms and pay whatever is convenient for them or sometimes subject to ethics committee advice. For the regulator, on the other hand, having unclear guidelines and viewing volunteers as rational actors is useful as they feel that they are no longer directly responsible for the outcomes of volunteer involvement in research in clinical trials as they are "rational beings" who make rational choices to participate.

The chapter has also shown how Schutz's system of relevances can be applied to the analysis of both individual and institution motivations. Like individuals, institutions too have motivations that drive their policies and responses to social issues. As shown in the discussions in the chapter, issues of topical and motivational relevance to institutions are shaped by the market-oriented context in which these institutions are situated. Response to issues of payment and other regulatory blind spots for example, shows how commercial motivations seem to influence regulatory responses on these issues.

In the following chapter, I explore the idea of rational actors further by looking closely at the demographics of healthy volunteers in the UK and their motivations for involvement in clinical trials.

Chapter 5
Who takes part in clinical trials and why?

5.1 Introduction

Demographic profiles for patient groups who take part in clinical trials are easily available. In the US, the Centre for Information and Study on Clinical Research Participation (CISCRP) has information on numbers of patients and their age, gender and ethnicity, but well-documented demographic profiles for healthy volunteers in early phase studies are not available in the UK. As mentioned in Chapter 2, while it is possible that CROs may have this information, it is certainly not available for public scrutiny.

In medical research, demographics are of vital importance as they help to structure and organise the recruitment process (Frank 2004). Precise demographic information (for example, assessing age, gender, employment and educational attainment) is key to successful research for pharmaceutical companies because it influences planning, distribution and marketing strategies. Having a highly accurate knowledge of the target population is also useful when developing educational and recruitment tools (McAllister 2009). More importantly, adequate numbers of volunteers are essential for robust evidence and wider testing of drugs (Frank 2004). A close study of clinical trial demographics also reveals disparities in representation of marginalised groups in clinical research and the ramifications of such unequal representation (Epstein 2008b). If no consideration is given to who takes part in clinical trials, then certain groups are bound to be exposed to exploitative recruitment; they may have little say in their protection from undue risk or exploitation and lack advice and support in the trial process. In most cases there is little understanding of problems that such groups face in terms of health experiences and the prevalence of certain diseases (Armstrong, Crum et al. 1999). Well-defined demographic data about healthy volunteers enrich debates about their involvement in clinical trials.

With regard to healthy volunteer motivations in countries like the

US, barriers to healthcare (Fisher 2007) are likely to be a motivation for taking part in clinical trials. In the UK, healthcare is free at the point of delivery. Therefore, the problems that such groups face need to be viewed in a wider context, in relation to social inequalities rather than only to access to healthcare. Some quantitative medical research has found that altruism and the desire to learn more about therapies are major motivating factors for volunteers (Aby, Pheley and Steinberg 1996; Truong et al. 2011). One study showed that access to health benefits during a trial was an important incentive for cancer patients (Nurgat et al. 2005). But social science academics who have explored motivations for participation in clinical trials generally agree that monetary rewards are the major motivating factors for healthy volunteers (Lemmens and Elliot 2001; Emanuel and Miller 2007). In a mixed methods study conducted in Brazil, it was found that the most frequently cited reasons for involvement in clinical trials were monetary benefits and access to health (Nappo, Iafrate and Sanchez 2013). Research cited earlier in this thesis (Abadie 2010; Fisher 2009) has also pointed to financial rewards as motivations for involvement. While these findings are encouraging signs of interest in healthy volunteer involvement in clinical trials, there has been little focus on the context in which these motivations become relevant.

In the literature review it was demonstrated that in the past subjects for first-in-human studies were often vulnerable groups, even slaves (Epstein 2008b; Hornblum 1999), and how this changed following the Nuremberg ruling, which outlawed the use of captive populations and encouraged the use of voluntary participants (Scocozza 1989). The introduction of volunteering brought with it other concerns to do with the exploitation of poor people desperate for money. Such individuals are thought to be willing to subject themselves to health risks in order to make a living (Abadie 2010; Petryna 2007). Even bioethics literature seems to consider healthy volunteers as coming from low-income households with low educational attainment (Hornblum 1998; WHO 1995), and who might be coerced into taking part in clinical trials. In the health promotion and bioethics literature there is a widespread assumption that people need more information and education to improve their health but also to make

informed decisions. Other literature on motivation examines why patients rather than healthy volunteers seek to take part in clinical trials; while this is useful on its own terms, the motivations for healthy volunteers' participation, which may potentially be altruistic as well, are very different from those of patients as they have nothing to gain in health terms. Where healthy volunteers have been considered, such studies have explored motivations using quantitative approaches to ask respondents to select pre-defined answers (Stunkel and Grady 2011).

This chapter draws on data from a survey questionnaire and interviews with healthy volunteers. The first part focuses on the demographic data drawn from my survey; the second examines the motivations for involvement using data from both the survey and interviews. Based on this sample, it seems that people who take part in clinical trials come from a variety of backgrounds – it is not just the poor who volunteer for FIHCTs. While financial rewards were an important motivation, there is a need to consider wider social circumstances and how they encourage people to volunteer. The chapter argues that socio-political, socio-economic and social structures should be part of the analysis if we are to understand why people take part in clinical trials.

5.2 Demographics

Data for this section were obtained from questionnaires that were used as a participant recruitment tool for this research. A CRO with over 80,000 volunteers on its register sent out questionnaires to healthy volunteers on its panel on my behalf and 187 healthy volunteers responded.

5.3 Results

Gender and age demographics

Of the 187 that responded to the questionnaire, only 122 healthy volunteers responded to the question about their gender. The rationale of the question was to find out if there are any gender differences in healthy volunteering. 42.6% (52) were male while 57.4% (70) were female, contrary to most research to date, which finds that risk-taking activity like that

associated with clinical trials is dominated by males (Byrnes, Miller, and Schafer 1999; Gardner and Steinberg 2005).

Respondents were asked to state their age; the hypothesis being that young people are more likely to volunteer for clinical trials. Again, there were 122 responses of which 4.9% were aged 18–21, 44.3% were aged 22–29 and the rest – 50.8% (62) – were between 30 and 40. None of the respondents indicated they were older than 40.

Based on the sample for this research it seems that the respondents volunteering in clinical trials were from a variety of backgrounds. First, contrary to observations that young men are more likely to engage in risk-taking behaviour (Byrnes, Miller, and Schafer 1999; Gardner and Steinberg 2005; Cohn et al. 1995), respondents in my sample were most likely to be 30 or older, followed by those in their twenties. There were only six 18–21-year-olds. It is also interesting to note that there were more female respondents in this sample than males. This challenges the view that risk taking behaviour is the preserve of young men because they are prone to feel invincible, reacting to peer pressure and searching for the "buzz" (Gardner and Steinberg 2005). However, clinical trials involve different levels of risk it is not clear what types of clinical trials attract which age and gender categories the most. The type of clinical trial chosen was not asked in the questionnaire but it was raised in subsequent interviews.

Education

I set out to find if clinical trials were topically relevant to the majority of healthy volunteers who had minimal education (secondary school or less). Sixty-five volunteers did not respond to this question. Of the 122 who did, 15.6% (19) had achieved no more than GCSE-level education, 37.7% (46) had achieved A-levels and 46.7% (57) had university degrees or higher qualifications. A chi-square cross-tabulation was conducted to find out if there was a correlation between level of education and willingness to take part in a hypothetical clinical trial if £1000 were offered for a five-night stay, despite potential risks. It found that 74.7% of those with a degree or higher qualification were more likely to express willingness to engage in the

hypothetical trial compared to 12.7% of both those with A-levels or equivalent and of those with GCSEs or lower. However, the difference was not statistically significant (P=0.375, X2=1.960).

Academic debates tend to reflect the view that taking part in clinical trials is more topically relevant for people who are uneducated (Horblum 1998, Cooper and Waldby 2014), so I found it interesting that most of my respondents had attained A-levels or a higher qualification. Though there may be sample bias, willingness to engage in a hypothetical clinical trial with above-average risks does not seem to be associated with educational attainment. This contradicts assertions that taking part in clinical trials is more likely to be topically relevant to people with low educational qualifications and challenges the prevailing view that lack of education leads to risk-taking behaviour. This view underpins most health promotion approaches and is central to the idea of informed consent in research participation in that provision of information is seen as educating the public so that individuals are able to make informed decisions. In Schutz's terminology, it would be considered aiding the interpretational relevance in the decision-making process.

Employment: income and dependants

The respondents were asked whether they were employed, in order to ascertain whether their socio-economic circumstances were topically relevant to the decision to take part in clinical trials. They were asked what they did for a living besides volunteering in clinical trials, in order to see if this makes taking part in clinical trials topically and interpretationally relevant (Schutz 1970). Fifty-nine (or 48.4%) of respondents worked full-time, 31.1% (38) worked part-time and 20.5% (25) were unemployed. It should be made clear that the question on employment concerned what the volunteers were doing at the time of completing the questionnaire as opposed to what they were doing at the time they started doing clinical trials, a question that was raised in interviews.

To ascertain whether working full-time meant financial security, respondents were asked to state their annual incomes. Eighty-three chose

not to state how much they earned annually, but among the remaining 104 respondents 18.3% (19) earned less than £10,000 a year and 19.2% (20) earned between £11,000 and £15,000. A further 14.4% (15) earned between £16,000 and £20,000, while 48.1% (50) earned more than £21,000 a year. There was no significant correlation between annual income and willingness to take part in a clinical trial if paid £1,000. This is not conclusive because there were many non-responses to the question on income and the sample size was small. The respondents were also asked to state whether they had dependants at home, the rationale being that for people with such responsibilities, taking part in clinical trials becomes topical because they might feel pressured to provide for their dependants if their incomes were marginal. The data showed that only 10.2% (19) had dependants. The survey found that there was no significant relationship between having dependants and willingness to take part in a clinical trial if paid £1,000 pounds for a five-day trial ($x2=2.519$, $P=0.284$).

The limitations of the sample were that it could have underrepresented the unemployed or people on low incomes and that it was too small compared to the population. Nonetheless, it was surprising that most respondents answering the survey were employed and earned around £20,000 annually, with 48.1% earning more than £21,000. The findings seem to challenge observations that healthy volunteering is topically and interpretationally relevant often to those who are unemployed or in low income jobs. Most of the respondents could well be earning incomes above the recognised level of poverty in the UK, which is defined as less than 60% of the national median income (Padley and Hirsch 2014). Rather, healthy volunteering is topical to people from a wide variety of backgrounds.

Nationalities and Ethnicities of healthy volunteers

Common assumptions, even among professional participants in this research, were that healthy volunteering was topically and motivationally relevant mostly to young, unemployed travellers, and that if they were British citizens they would probably be uneducated people from a working class background. In the words of Corporate Professional 2:

> The British contingent is more reduced to people who do not have jobs and to some people who can fit it among their working days. So some employed people and, um, some people who are technically unemployed but might as well be like musicians, actors who … in other words might not have consistent work to go to … Also it's changed a little bit over the years, as regards nationality … [Previously] a lot of this work was done mostly in students [though] the students have faded away [and been] replaced by… a large part of healthy volunteer[s] … those on one- or two-year working visas coming from the Commonwealth like New Zealand, South Africa and Australia. And … when the eastern European countries joined the EU, we then start to get people from the Baltic regions from countries like Lithuania, Latvia and also from Poland, Czechoslovakia, Hungary, Romania.

Most respondents to the survey were British citizens (77, or 67.0%), while EU nationals accounted for 18.3% (21) and British residents of non-EU nationalities accounted for 14.8% (17). However, care must be taken when looking at this result as non-Britons may not have responded to the questionnaire, reducing their representation in the sample, and people with immigration issues could have avoided answering this question or even avoided responding to a questionnaire probing their nationality. What is more, the questionnaire was sent out by a CRO. It is possible that cross-border healthy volunteering within the EU takes place but that was not shown in the responses. Regarding ethnicities of healthy volunteers, only 117 respondents answered this question. Based on this sample 75.2% described themselves as white Caucasian, with Asian Indians making up about 7.7%, and those who described themselves as mixed race making up 5.5%. Black Africans made up about 4.3%. The rest were small percentages of Asian Pakistani, Asian Chinese and African Caribbean. Likewise, the same practical considerations and observations apply here; results should be taken carefully as the sample may have been biased.

In short, the findings ran counter to widely held views of the topical and motivational relevance of healthy volunteering in FIHCTs. The images of poor, vulnerable and uneducated people taking part in clinical

trials did not emerge in the responses of the healthy volunteers in this research. Nor did they show that volunteers recklessly subject themselves to risks. However, the reality is that healthy volunteering is possibly topically and motivationally relevant to people from a variety of backgrounds, and my data suggest that reasonable numbers are educated and in employment. The significance of the findings is that they provide an opportunity to reassess understandings of ethics (Rajan 2006) in relation to people seen as vulnerable subjects in medical research and views about healthy volunteering in general. To do this we need to understand why taking part in clinical trials is topically, interpretationally and motivationally relevant to these rather unexpected categories of people. In the following section I focus on motivations for people's involvement in clinical trials using interview data to elaborate on the findings from the sample survey.

5.4 The reality: life events and motivations for getting into clinical trials

This section outlines how life events interact with socio-political and economic circumstances to make taking part in clinical trials topically and motivationally relevant (Schutz 1970) in people's decision to take part in clinical trials. By life events, I mean adverse circumstances such as ill health, loss of jobs and increasing debt, and their relevance in influencing individuals to become healthy volunteers in first-in-human clinical trials.

As observed in the previous section, contrary to common assumptions, healthy volunteering is not topically, interpretationally and motivationally relevant only to students, the poor and uneducated. Rather, the survey showed that some are educated and holding relatively well-paid jobs. This reality illustrates the complicated nature of the relationship between money and social circumstances. Research suggests that that people who are in debt take desperate measures, borrowing more money and getting deeper into debt (Kamleitner, Hoelzl and Kirchler 2012; Montgomerie and Williams 2009). Recently in the UK, the government brought out policy directives to address growing levels of over-indebtedness among certain groups (Wallace 2012). The same may be said of people who take part in clinical trials: in the economic downturn, many

have lost their jobs and livelihoods and have failed to find other work. Some believe they have no choice but to volunteer for clinical trials.

Monetary reward as motivation

From the data in this study and from the literature (Stunkel and Grady 2011; Emanuel and Miller 2007), it is clear that for most respondents money is the motivational relevance for getting involved in clinical trials. That is acknowledged by most of the healthy volunteers and professionals who took part in this study, as the following extracts show.

> The money is very important. If they put something in my body, they have to pay me (HV 9).

> Obviously for me it's about the money. That's why I am doing it (HV29, aged 25 self-employed, media).

> Well, it is obvious that these individuals get involved in our studies because of the money that is on offer. That is mainly the reason (Corporate Professional 1).

This is also supported by findings from the questionnaires. The respondents were asked to answer a series of hypothetical questions. When asked how strongly they agreed or disagreed with the statement "Monetary compensation was important in my decision to take part in clinical trials", 51.2% (62) agreed and a 38.0% (46) strongly agreed with the statement compared to 0.8 % (1) and 4.1% (5) disagreeing and strongly disagreeing respectively. The respondents were also asked how extremely likely or extremely unlikely it was for them to take part in clinical trials if there was no monetary reward. Most of the respondents were not willing to take part in clinical trials if payments were not included. 52.8% (66) stated that it was extremely unlikely and 23.2 % (29) that it was unlikely compared to 1.6% (2) and 4.8% (6) who stated they were extremely likely and likely respectively, to take part without payment. The remaining 17.6% (22) were unsure. Of added interest was the fact that though the survey sample may have been biased, even higher-income respondents acknowledged

monetary reward to be a strong motivation.

Most discussions about motivation for volunteering in clinical trials stop at this point, acknowledging that people are motivated by financial rewards and then adding a list of other reasons that include altruism. As Fisher (2007) observes, such studies tend to see volunteers as individuals who willingly come forward when invited to take part in clinical trials. Such views of willing subjects are in keeping with the concept of individuals as rational actors, a topic covered in detail in the next chapter. A problem with such a view is that it results in a smooth narrative of motivations which negate the contexts and circumstances of people's lives and their relevance for people's motivations to volunteer for clinical trials. Relationships between money, the body and risk taking are complex and often contradictory; decisions to take part in clinical trials often involve a system of relevances (Schutz 1970; Bloor 1995) rather than a simple cost-benefit analysis. Corporate Professional 1 saw it this way:

> I think … that money has different significance to people who are in different life situations. So if you are struggling … um, or let's say if you come from Poland, a small amount of money in this country, if you send it back to Poland … uh … can buy a lot more, and similarly for other eastern European countries, maybe South America, too. So there is more of an inducement for people in certain situations.

Understanding healthy volunteering in FIHCTs requires looking beyond the signed consent form to explore wider issues that can otherwise be taken for granted (Schutz 1970; Bloor 1995). This involves presenting both the contradictions and similarities in people's explanations for motivations. In the following section, I consider how different factors shape people's motivation for involvement in clinical trials.

Financial crisis

For most of the respondents in this project, volunteering in clinical trials was not something they wanted to do. Rather, it became topically

relevant because they considered their financial situations to be beyond their control:

> I was in some debt that really needed to be paid off, otherwise I was going to be in some shit if I didn't, you know. So it was kind of a situation where I had to do that to get myself out of the sticky situation I was in (HV4).

> The first one that did I [pause] um, I think I was in a sticky situation, just out of a job at the time, and I needed a little bit more extra cash obviously to survive and it was a good way to make, a quick way to make big sum of money, and yeah [laughs] (HV1).

Before becoming involved in clinical trials, volunteers usually tried other options, such as finding a job. In Schutz's framework, this would be interpretive relevance. This either failed to solve the problem, or there was no job to be had. It was at this point that clinical trials become motivationally relevant. Even some of the respondents who had jobs believed that their earnings would not solve the problem and that it would take a long time to pay off the debt.

> At the time, I had a job, the pay was good and everything and I had some debt that I had to urgently pay off. I would never have managed to pay off the debt if I had relied on the job so the only way was taking part in a trial (HV 11).

> My main motivation is to help me with things like fees, accommodation and things of that sort associated with my life at university. You know, I can't afford to pay these fees if I just worked the regular student jobs. So I got started after I decided to retrain after losing my job in Ireland, so you know, I had no savings to pay for fees and things like that. So this for me is a good way of meeting those demands. I have tried looking for jobs. I just can't find any (HV25).

HV9 said he "had no choice" but do clinical trials. He had been unemployed for a long time, he could not find a job and his debts were mounting up.

Also of interest is how participants use accounts of their social circumstances as topical and motivational relevance for taking part in clinical trials; their decisions seem intended to deflect criticism for risky behaviour:

> I was in a transition of my life. I had left my home country, Brazil, lived in Europe but could not find a job and then came to the UK. During that time I was unemployed and was, well, let's say I was struggling financially and I didn't have much of a choice but to volunteer in clinical trials because I badly needed some money to pay bills, rent etc. I also had credit card bills to settle that were going out of control. I looked for normal jobs but couldn't find any. You know, it was really hard situation for me (HV9).

HV12 had a job, but spoke of the temporary nature of jobs such as modelling and acting, which involve short-term contracts:

> I do clinical trials when I am not on set to supplement my income. As you may know, work in my field can be erratic, so, yeah. So at the time when I decided, right, I am just going to have to do this, bills were creeping up and I just needed to, you know, get them sorted ASAP. I tried other temping jobs but it was going to take too long to get them paid off (HV12).

Some respondents would deflect imputations of greed by emphasising that they were in such dire financial straits that they had no choice but to take part in clinical trials. Others said they volunteered for clinical trials in response to media adverts or after friends had told them how much money they had earned in a short time.

> I started taking part in clinical trials in 2006, because at the time my friend was doing this. He told me about

> clinical trials and how much money you can make in a short time, such kind of thing, and then I registered (HV9).

> Well, my boyfriend started first, so he told me about it [pause] and [pause] told me that it was safe and that it was a good thing to do … [I] thought it was an opportunity to help other people [winks] and make some money at the same time [laughs out loud at the mention of money]… yeah! (HV6).

The participants who had heard about clinical trials from friends or relatives talked of how easy it was to decide to volunteer. For them the trust they had in the individual who was encouraging them was crucial. Such participants seemed to have little problem transitioning from topical to interpretive relevance as they had the assurance of someone they trusted who was not a medical professional. It is interesting to observe here how lay accounts and experiences of health and risk can influence decisions and behaviour.

For others, it was encounters with advertisements or media reporting that made clinical trials topical and interpretively relevant. The Northwick Park incident aroused widespread interest (topical relevance for some participants who noted how much reward had been offered to volunteers in the trial).

> To start with, I got interested in trials after that one that went really badly wrong [Northwick Park]. It got me thinking so I started to look out for more trials. This one they actually contacted me. There are a number of websites such as trials4us.co.uk … you fill out, like, a basic application. You say how old you are, whether you smoke, you drink, if you take exercise regularly, um, if you have any abnormal conditions, like wear a pacemaker. (HV 7).

In general, the preceding discussion illustrates how monetary rewards coupled with their personal financial circumstances made taking part in clinical trials of topical relevance to some healthy volunteers in this

research. Participants talked of considering other options to resolve their financial problems, which upon interpretation made monetary rewards in clinical trials a motivational relevance for taking part in clinical trials (Schutz 1970). The financial situation of some respondents was so serious that they felt they were caught "between a rock and a hard place". Nevertheless, the decision to become clinical trial volunteers was not easily taken.

> I had not worked regularly during that particular year and bills were alarmingly building up, you know. So it was a must-do-something situation for me because I couldn't bear the thought of what was coming if I hadn't done something at that time. Not that the decision was easy to do this – both options were hard. It was like bite the bullet and live, or fall of the cliff or face the hungry beasts, that bad … you know, but like a short stop-gap (HV 30).

Most participants did not intend for clinical trials to become a regular practice; it was rather an impromptu response to a situation thought to be running out of control.

> Oh yes, I did not have the job at the time … So I got into this [volunteering] you know, as a sort of, um, one-off solution, um, like last resort but not to be done again, that kind of thing (HV5).

> I would never have managed to pay off the debt if I had relied on the job so the only way was taking part in a trial … At the time the pay was good enough for me to cover for that. I did not intend to do a trial after that, though … It was intended to be a one-off thing, pay the debt and move on to normal life (HV13).

One case that deserves mention is that of a new immigrant who was forced by the man she was in a relationship with to participate in clinical trials. She was warned that if she dropped out of the trial without being paid or talked to anyone she would be beaten or reported to police and deported.

Fearing for her life, she took part in two clinical trials and could not even tell the research team of the threats. This case is an extreme and hopefully rare occurrence.

> I didn't know anything about clinical trials before then … I was just taken into this (trials unit) by somebody. It was like … I had to do it, not that I wanted to do it … It didn't have anything to do with a lack of a job on my part because he needed the money. I was forced into doing two clinical trials. This person needed the money and registered me and took me to this trial centre and took me in, and waited outside … I was so scared (HV 3).

However, the shared sense of "no other option" in the accounts above should not be overlooked. It seems whether coerced by someone or by social circumstances, participants in this research felt that taking part in clinical trials was the only way out of their problems.

Continued participation in clinical trials is examined in Chapter 6. However, the preceding discussion about the role of financial pressures and incentives can be linked to the demographic make-up of healthy volunteers as outlined in the first part of this chapter. It was observed that the demographics of people who take part in clinical trials are not what we have been led to believe either by popular discourse or previous research. In the survey for this research healthy volunteers were mostly aged over 25, and in their explanations for taking part in clinical trials they list being unemployed and/or in debt. But also the sample bias alluded to earlier in this chapter would have contributed to the accounts given by participants. However, the findings show how periods of unemployment, unpaid bills and rising debt can combine to make taking part in clinical trials topically, interpretively and motivationally relevant (Schutz 1970) for some people even when they subsequently have paid work. These situations the respondents may find themselves in explain why certain groups of people take part in clinical trial. Looking at healthy volunteers in this way, therefore, challenges the presentation of healthy volunteers by what Fisher (2007) observes as being the portrayal of healthy volunteers as "willing" or

"ready to recruit" participants and sheds light on how their financial vulnerability makes them available for research.

On the whole, the participants seemed to take a "pragmatic" approach in response to social situations they felt needed to be addressed as quickly as possible. For them, failure to do so would have seen them faced with serious problems such as fear of violence or bailiffs at the door. These individuals had to do something to avoid the consequences of continued financial problems that seemed to be spiralling out of control. Reviewing the respondents' reactions to difficult situations reveals how their actions are shaped by normative conceptions about unacceptable responses. Some saw their attempts to find jobs as a response to social definitions of acceptable sources of income and taking part in clinical trials as morally suspect:

> Mwale: Are you saying they [parents and family] were morally judging you?
>
> HV 22: You can see how that was linked to work and what they thought was good use of my time … [they] were sort of anxious that I was putting myself in harm's way by doing clinical trials and not looking for normal job.
>
> I just felt violated … what's worse I couldn't tell anyone doing trials, I just didn't want anyone to know, because they think I am just careless or not keen on getting a job (HV3).
>
> Look at me, someone like me with a master's degree would have a reasonable job (HV29).

These comments link concepts of morality and motivation to what society deems acceptable ways of making a living (Forsyth and Deshotels 1998). Taking part in clinical trials is considered to be something that reckless individuals do; for most of the respondents, taking that step was difficult. This challenges common perceptions of volunteering as dubious

morality and risk-taking behaviour. In the extract above, HV29 implies there is something shameful about being a volunteer when one has a master's degree, confirming that s/he took part in clinical trials because of circumstantial pressures. But more importantly the "look at me" statement demands that we move beyond a focus on stereotypes to consider actual social class origins, including educational attainment and social status and identity in order to understand why people take part in clinical trials. Furthermore, the invitation "look at me" also seems to suggest the individual feels this should not be happening to him/her or that people who share their characteristics do not normally take part in risky behaviour. It is here, therefore, that morality as part of healthy volunteering becomes evident.

Health crisis in the family and heath checks as motivation

For some respondents, taking part in clinical trials was prompted – and became topically relevant – not only by their financial problems but also by setbacks in other areas of their lives, such as the declining health of a family member. Such crises seemed to intensify the realisation of their own fragility. Taking part in clinical trials was a solution – in addition to earning money, they would be medically examined, increasing the chance of early detection of a serious illness. Their motivations were less altruistic than personal, and even selfish. Asked if they would take part in a clinical trial for free if invited, one replied:

> I think my dad had just been diagnosed with late onset diabetes which really affected him badly, so I was starting to think more about my own health and worrying about things that I did not know about my health that could be, you know, going haywire. So I thought doing such things would provide an opportunity for them to do a test, like an MoT [Ministry of Transport check for roadworthiness] like on your body, you know. You see, because I see my body as such [a machine], I started thinking, you know, just in case I may need something, a part of me that needs oiling, you know, and I wasn't aware of it (HV22).

Of course, one could always go to a GP for a check-up, but some respondents thought that GPs would not have enough time to examine someone without an obvious illness. They preferred clinical trials to accessing primary care because they felt that the nature of encounters with the GPs meant that they could not be thorough enough or have the time to see them if they did not have any physical illness. Healthy Volunteer 25 shared HV 22's view of medical check-ups:

> … like a car MOT, you know [you] can get that from your GP but it's something you have to push for. Besides, I don't think they [GPs] can do it as often as I would like to have it done for obvious reasons, you know, time and budgets. You also get a sense of rushing when you are talking to GPs but in hospitals on a trial, it's more thorough (HV25.

> … but GPs are not thorough. They have 15 minutes and then you have to wait for a long time before you could hear back from them. It's not just worth the time and they may not tell you more about the results either (HV22).

> [the]…initial "screen" prior to a study can be like an MOT, it usually acts to reassure me that things are generally OK [in the body] before I then take the plunge and accept the trial. Which is odd as I rarely visit the GP, so I suppose this "screen" acts as my check-up. Not sure if that makes sense. Because GPs are generally slow and the procedure is just cumbersome … but on the clinical trial it's thorough and quick (HV13).

> So I kind of get [my health]check but also contribute to helping someone at the same time if the drug is developed kind of thing (HV14).

For one participant, the decision to take part in clinical trials came about after a family member wanted a child but was struggling to conceive. This made the participant think about issues in a broader sense:

> I guess partly the reason I started doing the studies that I am doing now is that it was about a fertility study … at the time my brother was having his first child after some struggles so I was kind of attuned to it a bit more (HV1).

This section illustrates that although people appreciated the reward on offer in clinical trials, some were also willing to do clinical trials for some kind of health benefit. For these people doing trials was a way of dealing with uncertainties about their health. For others the trial was a way of checking on their health along the lines of what they called a body "MOT". The family problems included, among others, health problems of genetic origin or those that might arise if they did not check their health status regularly. For one participant it was health issues experienced by other family members that prompted them to think of taking part in clinical trials. For these respondents, in addition to debt and unemployment, health issues were a motivational relevance. Analysis of the accounts in this section shows that participants saw taking part in clinical trials as a way of avoiding risk rather than taking additional risks. Also of interest is how the accounts seemed to be used as a careful way of claiming altruism as can be seen in the last quote. This is interesting as participants felt that this was a justifiable way of engaging with risk.

Biographical situation

As in the preceding section, for a minority of participants, in addition to financial rewards, their biographical situations also had motivational relevance for getting involved in clinical trials. In using "biographical situation", I refer to Schutz's analysis of how one's socialisation provides the basis for beliefs, views and knowledge of the world around oneself. For some respondents, taking part in clinical trials was an opportunity to act on their beliefs, as expressed in the quote below:

> … also, I do clinical trials because I do not believe in animal testing, so you know, you can't be against something if you cannot come forward and do

> something about it. So I am interested because I want to do my bit in stopping animal testing. Animals should not be used to solve our own problems that we bring on ourselves (HV12).

This seems to be a different expression of altruism, one of "doing one's part" to develop safe, effective drugs while protecting animals. Another volunteer was motivated to take part in clinical trials to achieve certain personal goals and to use the opportunity to build contacts, particularly with medical researchers, in a chosen field of work. Others chose to participate because of their interest in the role and function of medicines in the developing world.

> … So yeah, it's not just about the money … well, I do need the money badly, obviously… I want to work in clinical trials in the future so I hope to build contacts but I feel someone has to help others and at this time I feel it's my turn to do that [volunteer in the clinical trial] (HV15).

> It's not just about the money [laughs] … it's also about helping others to some degree. Medicines are needed everywhere in the world to help the sick so I play that small part in a way (HV 12).

Some of these accounts are noteworthy for the undertone of self-justification. The respondents did not want to be stereotyped, but rather to be viewed as reasonable people with varied interests and aims. Most of the interviews were done in public spaces and possibly the participants would have wanted to be seen in a positive light, especially when being asked questions by a stranger, as I discussed in chapter 3 (Callon and Rabeharisoa 2004; Will and Weiner 2014) (see p. 114). Others rejected the idea that they had to justify themselves in any way. They stated clearly that their involvement in clinical trials was purely for the money.

> I do this and others do it purely for money and if anyone says otherwise I disagree, it's bullshit excuses. People do this for money, not to help science or

> develop medicine. This is like any other job, you give in your day's work and they pay you. I actually find it annoying when people talk to me about my volunteering in medical trials and make me feel like I am a lazy, selfish person … it is hard work doing clinical trials (HV4).

Of interest here is that the participants questioned normative assumptions about "normal" ways of earning money (West 2000; Forsyth and Deshotels 1998).

On the other hand, healthy volunteering can constitute resistance to social expectations as people get involved in what is normally seen as a risky and even reckless venture and in so doing challenge these social expectations of acceptable ways of earning a living. This is an aspect of the "moral economy" (Scott 1977; Edelman 2005; Daston 1995) and positive public views of risk taking (Lyng 2009), discussed in Chapter 2, that relates to the desperate nature of volunteers' social situations and circumstances – their conception of work and social justice, what it takes to survive in a market economy, and how these factors interact to drive them to risk their health. To understand better why people become involved in clinical trials requires accepting, first, that their decisions are dictated by the need for survival. Then one should investigate the interplay of relationships and encounters with the state, professionals and corporations on one hand, and interactions with family and society on the other. These interactions are analysed for their relevance in driving, influencing or obstructing involvement in clinical trials. Obviously this means reframing a range of issues, notably trust between experts and lay public, and informed consent, which are examined in greater detail in Chapters 6 and 7.

Scott's concept of "moral economy", introduced in Section 2.4, can be applied to people – individually and not collectively – who decide to volunteer for clinical trials. The healthy volunteers in this research held strong beliefs about the right to have enough to survive as independent individuals. They also wanted to live up to social standards of acceptability and to avoid the shame associated with failing to earn enough. They also

demonstrated an antipathy to the risks (Peretti-Watel and Moatti 2006; Peretti-Watel et al 2007) inherent in participating in clinical trials. For most of the respondents, the goal was not to become rich but rather to avoid the problem of unemployment and the shame of being unable to support themselves (and possibly their families). Therefore, to construe healthy volunteers as aspiring to become rich fails to appreciate the reality of everyday dilemmas in their quest for survival in a market economy.

Scott shifts resistance from the periphery, where it is likely to be viewed as the actions of a few disgruntled individuals, to the ways in which society produces certain forms of agency. The surprising findings in the above analysis of the demographics of healthy volunteers may reflect the nature of the market economy, which flourishes amid the widening gap in incomes and increasing social inequality (Stiglitz 2012). Increasing unemployment among graduates means that many approach their 30s with inadequate incomes and without a job. The high cost of living in London, where most of the participants in this research are from, could also qualify what a "reasonable" income might mean for different people.

The participants' desire to live up to social expectations and having an "acceptable" job is of interest here, as it shows up the contradictions in market-oriented economies. While individual liberty should be protected from undue state and outside interference (Sen 1993), liberties are also subject to social definitions and expectations. This may explain why most of the participants in clinical trials in the sample surveyed in this research were in their mid-20s to their 40s. As most people in this age category could have been at a stage in their lives where, for instance, they should have had a house, a stable job, among others, which at the time they probably did not have hence taking part in clinical trials becomes a way of keeping up with expected standards. However, it is also possible that the bias in the sample of this research would have contributed to the over representation of people in these age categories. Nonetheless, having insufficient income is undesirable and thus taking part in clinical trials becomes motivationally relevant. This raises the questions of what is meant by vulnerable subjects, and how this relates to ethics. The positioning of

volunteers as vulnerable is clearly an ethical issue. The definition of vulnerable people in ethics and legal guidance in relation to healthy volunteering focuses on mental and physical abilities (Lemmens and Elliot 2001; Fisher 2007). Important as these may be, there is no additional consideration of the social circumstances in which individuals find themselves and how that contributes to their vulnerability. Instead, the idea that someone with a sound mind should be able to make a decision is used to guide definitions of vulnerability. The ethical, political and economic nature of clinical trials is typified by the variety of players, from wealthy corporations and government institutions to ordinary citizens (or non-citizens). Addressing ethical concerns in such settings requires a broad concept of ethics that takes into account the interactions of regulatory and clinical trial processes between these players as well as the power relations, including economic power, that characterise such interactions. Using Schutz's system of relevances, there is a need to analyse how these interactions are structured and how they in turn structure ethical views about who is considered vulnerable and to whose advantage it might be to consider certain people vulnerable and others not.

5.5 Summary

This chapter has looked at the demographics of healthy volunteers in FIHCTs. The findings from the data showed that many healthy volunteers were educated and held well-paid jobs, challenging assumptions that it is mostly the unemployed, students and young people travelling through cities like London who take part in clinical trials. The healthy volunteers surveyed in the sample came from a variety of backgrounds and most of them were in stable employment at the time of volunteering.

It was clear from the accounts cited in this chapter that monetary reward was nevertheless the major motivational relevance for getting involved in clinical trials, but motivations were shown to be much more complex than just a desire for quick money. Most of the respondents acknowledged that they had volunteered mainly to address their financial problems; they had failed to find other solutions and believed that their

only option was to take part in clinical trials. Others, asked about their motivations, seemed keen to justify their choice and gave other reasons for having participated in the trials. Some did not wish to be seen as reckless; others saw taking part in clinical trials as being like any other job. The participants generally seemed to reject the notion that they had "volunteered".

I argued that healthy volunteering is a means of survival for most participants, and that conceptions of vulnerability in legal and regulatory discourses should therefore be broadened to include people who may be financially disadvantaged. The argument highlights how regulation and ethics play a role in defining agency and legitimising certain forms of agency. Drawing on Schutz's system of relevances, the chapter has also shown how institutional contexts of personal debt, rising costs of living and unemployment act as topical relevance for individuals resulting in healthy volunteering becoming a motivational relevance. The participants in this research talked of looking for conventional means to resolve their financial problems (interpretational relevance), before deciding to take part in clinical trials (motivational relevance). In addition, looking for other options before taking to healthy volunteering is in keeping with what Bloor (1995) calls the "polythetic" nature of decision making in which individuals explore various possible options that may be available as a response to social stimuli. Furthermore, the participants' accounts of unemployment and debt among others as precursors to healthy volunteering (becoming topical relevance) illustrates how relevances may be imposed by wider socio political and socio economic contexts. Using this framework has shown that understanding healthy volunteering conceptions of risk requires the researcher to look beyond the concept of rational choice or cost-benefit analysis theories. In the following chapter I consider healthy volunteering in the context of economic and gift/altruism exchanges.

Chapter 6
Economic Exchanges or Gift Relationships? The Body in First-in-Human Clinical Trials

6.0 Introduction

This chapter examines the complex nature of the relationships and interactions that take place in clinical trials. I analyse how volunteers and professionals view clinical trials, whether as an economic or a "gift" exchange. The success or failure of early-phase or FIHCTs relies to a great extent on the recruitment of sufficient numbers of suitable participants (Mirowski and van Horn 2005; Fisher 2007a). The introduction of laws and regulations governing the use of human participants in medical research in the 1970s brought about a shift in the conduct of clinical trials: seeking consent from participants meant that from this point participants could only be volunteers (Bolton 2005; Mirowski and van Horn 2005; Hedgecoe 2012). The literature review discussed how changes in these policies and the desire for a fast turnaround of results saw a growth in contract research organisations. CROs pride themselves on being effective, efficient in recruiting the right kind of people and competent in managing studies. Recruitment of participants has become a lucrative business for the CROs and has brought economic gains for countries where such research takes place. The increasing numbers of CROs has intensified competition in the global search for healthy volunteers and increased the rewards for participating in clinical trials.

In the same way that the previous chapter problematises the idea of an "autonomous volunteer", this chapter questions the notion of "altruism" in healthy volunteering. The chapter examines the following topics: financial incentives in healthy volunteering; how regulators and managers of clinical trials view healthy volunteers; how healthy volunteers view their bodies as valuable assets; ways in which the body is commoditised; and the gift exchange in healthy volunteering.

6.1 Becoming "valuable data"

Participants in this study spoke of noticing a change of attitude on the part of the research teams once they were admitted into the trials. The experienced a sense of being depersonalised and institutionalised, in an echo of Goffman's (1961) concept of "total institution". Being recruited for a clinical trial is fairly easy as outlined in chapter 1; it simply requires entering one's details online, receiving an advertisement and expressing an interest in one of the clinical trials being advertised, and then being called in for an assessment. The assessment confirms whether the individual fits the requirements of the study in terms of height, weight and other vital signs. It is upon admission into the trial that participants experience "becoming data". By this they referred to the changes in the way they were treated, pre- and post-admission into the clinical trial. This process is closely linked to the sense of becoming depersonalised and institutionalised.

Depersonalisation and institutionalisation

Depersonalisation refers to a loss of subjective identity, feeling that one is reduced to being a mere component in a system (Hochschild 2003; Tracy 2000; Goffman 1961). The concept is linked to what is commonly referred to as "biovalue" (Rajan 2006; Cooper and Waldby 2014), or the way people are seen in terms of the value of their biological mechanisms. Most participants described their experiences during clinical trials as dehumanising.

> … I think the other issue is that trials, once you enrol, you become just a number; you are just there, you are not you. So it can be quite hard to deal with sometimes, and the powerlessness as well … because basically to them you are just data, you know, but have value in the form of data and the money it represents, not the human being I am (HV19).

Some participants spoke of "becoming a number" or "becoming just data" and feeling loss of identity; others of feeling like laboratory rats:

> … I also felt much like a laboratory rat, like a testing animal, especially when you are not treated well by the nurses …Sometimes you are treated like a number on their sheets and not a person … (HV9).

> … to them we were just numbers on hospital beds and not people. It's quite strange, not that it was obvious, but in subtle ways. But you know, it does really feel that you are just a specimen on the trial (HV 12).

> Yes, I felt abused, like I am a secondary human being. Like, ah, like, um, not even a human being, like a lab rat. And it's quite extreme and it goes against all of my objective reasoning – that kind of emotional, rational feelings … because I know that I am a human being, there are other human beings and that we are different but we are all equal. But this made you feel unequal. It's like while you are in that experience and this kind of emotional feeling I had afterwards was very … it's very strong … it's very arbitrary. It's not something that I believe, um [grimaces] … I felt really, like, insane, like quite mad (HV5).

The depersonalised nature of such experiences is significant in two ways. First, for the participants this demonstrated the economic nature of healthy volunteering and how healthy volunteers become commodities. Volunteers felt they no longer had control over what happened to them and realised that their feelings would not be taken into account. Second, they experienced a loss of power and control and felt like unequal objects, their humanity unacknowledged. The research team controlled their movements, diets and intake of food and contact with the outside world. The participants were given a rigorous schedule detailing every procedure, minute by minute, which added to feelings of powerlessness and the challenge of enduring the procedures they were subject to. However, not everyone experienced these negative feelings:

> I am fascinated by medical research … but … you must go in ready to deal with that mentally before going in,

> also be ready to cope with the food because it's not pleasant food. So go in ready to eat shit food (HV11).

> … So I go into trial ready to deal with whatever comes so I don't feel used at all and I don't mind those who try to boss or their rules, because I go in mentally ready … and it does not bother me … I mean the research team or their rules. I am also captivated by science, so that gives me a chance to see it close by, you know (HV 18).

These two participants were evidently so intrigued by the processes involved in the clinical trial and so prepared mentally for the experience that the power dynamics were of relatively little concern.

Institutionalisation refers to ways in which individual behaviours and actions are defined and limited by an institution (Goffman 1961). While a small section of the participants found relationships during the trial to be cordial, each day was structured strictly around fixed rules. They were given a schedule detailing every procedure, minute by minute. So in addition to being depersonalised, and perhaps as part of the depersonalisation process, they were subject to in-house rules that were non-negotiable. The participants felt that by this time they had been reduced to being a small yet valuable part of the clinical trial.

> … They are just interested in my body and the results that my body will give them. After which they will discharge me and they will not be interested in what happens to me. They kind of dehumanise you in many respects. But they also have a lot of power over you. It comes in different ways, like you know, they do what they want to your body at any time but also you have to eat all your food and there are no negotiations. It's like you've signed over all your control of things … besides you know we don't have a choice of food. You eat what is given to you (HV9).

It should be pointed out here that the depersonalisation and institutionalisation did not take place separately; rather these occurred

synchronously in the clinical trial process. Dealing with the changes associated with becoming institutionalised made the situation "topical" and so participants started to think of the institutional motivational relevance to justify certain rules and actions that were being imposed. This relates to Schutz's view that the relevances and subsequent actions people take can also be imposed. Coming to terms with rules such as "you must finish the food given to you", regardless of whether they liked it, the participants found themselves thinking of the reasons, or interpretations, of why the research team would impose such rules. The participants generally took a non-questioning and non-critical approach to dealing with the situation and became resigned and compliant.

> The food was absolutely awful. I wouldn't give that food to a dog, but I couldn't question that. I thought maybe it was part of the trial or that surely they wouldn't give us such food for no reason. They must have had a logic for that (HV29).

> I did not understand why I couldn't be allowed to access my makeup or such small things. I thought maybe it was safety, but it was really bad. But I thought they had a rational reason for that. It's stupid, thinking about it now (HV13).

> [What] was really strange is that I felt like a novice. Some people are really used to doing this and they did not see the problems that I saw. They seem to be coming regularly for trials, something which was quite unnerving for me (HV 12).

Some participants were shocked by this shift in the way they were perceived. One participant who had experienced an illness which required medication from the GP was eliminated from the trial. Instead of receiving sympathy from research team members, she said, they were displeased that their trial data and results had been affected.

> … they were not pleased that I had fallen ill and [was required] to take antibiotics and therefore I could not be allowed to take part in the trial. It meant that they couldn't get their results … You could see the disappointment on their faces because I was going to drop out of the trial …no sympathy for me at all … These doctors, they are looking for results. They are paid for their results and so the focus is on the results, and by that I mean positive results, and so they will not tolerate anything that will spoil their outcomes. Otherwise, their product will not go to the market (HV5).

The above quote and preceding discussion illustrate ways in which, by taking part in clinical trials, healthy volunteers became valuable data for the research. In doing so, they were subject to rules, regulations and study regimes that ensured the data was not compromised, which is of motivational relevance to the institutional (Schutz 1970).

6.2 Negotiating personal interest and company procedures

The changes in the way they were viewed by the research team gave the volunteers different ideas of what it means to be a good volunteer. For some, being a seasoned volunteer meant being able to put up with the situation and its consequences; the changes in the way they were viewed were seen simply as risks of the trade. Healthy volunteers tended to look down on fellow participants who were, in the words of one, "fussy about things". Participants who insisted on better treatment found themselves isolated while their colleagues simply got on with things.

> … I just couldn't cope with her [talking about another HV]. She was always bitching, moaning, whining and complaining about everything from 6 to 6. We had a few words, you know … because you see, if someone decides to come on a trial you must be ready for what it brings (HV11).

The "ideal" volunteer, therefore, was one who could cope with the situation without feeling inconvenienced by aspects of the clinical trial.

Volunteers who complained were often looked down upon. A lack of reaction to the challenges was often seen as mark of experience in doing clinical trials. This is linked to Lyng's (2009) view that today risk taking is viewed in a positive light. Of interest is how being in such situations produced different types of agency among volunteers. Some questioned the rules and restrictions; others accepted the status quo. Most participants were aware that there were forums for airing grievances but they believed that their complaints would be ignored because the staff members to whom they would complain were responsible for administering the trial. The topical and motivational relevances of the staff were seen to be protecting the interests of the companies they worked for:

> let's face it here, their aim in the trial is to pass the drug and market it to make money from it, … others [staff] are absolutely obsessed with their positions of power. They are, like, this is a scientific trial, this is, and they didn't care what you felt … some staff did make sure you felt that way. If I met some of them in my life outside of the trial, I would have words with them. I would say, "That was not acceptable, the way you treated me or spoke to me". The thing with the trial is that they do dehumanise you, you sort of become a number on their sheets and not you anymore and that is very painful to take (HV29).

It was clear to many participants that they had become valuable objects of research even while they were devalued as human beings. The participant's view that they would have a word with one of the researchers outside of the clinical trial is very telling; the power context of the trial itself prevented the participant from airing those views during the trial itself. Some participants said the research teams had downplayed volunteers' unpleasant experiences because it was bad for business to have documented evidence of complaints or extreme side effects.

> … yes, they said that: "Okay, tell us if it gets worse", but you know, they said they keep a close eye on you and they said, "We will look at you" … they try as hard

> as they can to keep the trial going because if they do tell this [about side effects] the trial may be cancelled … If not, I mean, they can't stop trials going bad – you know, it may hurt their business or profits (HV 25).

Staff members were often seen to come up with "tactics" to keep the trial on track, as HV 29 found when experiencing side effects:

> They tried to explain what we were feeling, saying it was psychosis and that's what the psychiatrist on the ward said to us. So I was like, confused, because we went in there without any such problems and when we felt the drug effects, we were diagnosed with psychosis. I think it was a tactic for them to try and ignore the effects we were feeling, because obviously their aim is to pass the drug and market it …, and if they can try and explain away as much as possible of the side effects, they may then continue to the next stage, because if they report extreme effects they may have to stop the trial.

The complex nature of the transactions that healthy volunteers have to negotiate in clinical trials is clear from the foregoing extracts. The process of becoming a "data point", involves depersonalisation and institutionalisation coupled with the loss of control or power over what happens to their bodies. They lose their identities, becoming mere research data, yet valuable assets on whom the progress or failure of the trial depended.

6.3 Market exchange?

As the participants' value in the eyes of the trial team changed, some of them came to see their involvement in clinical trials as a market exchange, by which I mean that the healthy volunteer's body is exchanged for monetary reward offered by the research company. The healthy volunteers' topical and motivational relevance was the monetary reward; the corporate motivation was the value of these participants for research (Schutz 1970; Douglas 1987). The economic and symbolic value of the FIHCTs is made explicit in the Nuffield Report (2011) on donations of

body parts. In addressing the role of healthy volunteers, the report talks of mutuality in the exchange between volunteers and CROs – both parties gain benefit from the relationship. The report recognises that volunteers have a significant role and acknowledges that they have an interest in the result of the research (Nuffield Report 2011). Human involvement in clinical trials is seen to be part of the "bio-economy" (Cooper and Waldby 2014; Waldby 2000; Rajan 2006). Cooper and Waldby refer to healthy volunteering as a form of labour, although it is not usually considered as such by the industry.

In interviews, the participants spoke of ways in which the value and nature of the exchange were made explicit during the trials.

> … and it's part of the things you sign up for and I am aware of what is being used of me and I am aware of what I am taking away from them. So I was equally aware of the fact that it's some kind of a transaction here (HV29).

The volunteers were well aware of the nature of the contract they had agreed to. HV14 replied to a question about why people take part in clinical trials:

> I think the money is the motivation for everyone. I don't think the people volunteer for the sake of science or health concerns. I think if you take away the money, I think the number of volunteers will shrink extremely.

> [Money is] … very important I don't buy the idea that it was to help science or help people. I just wanted the money and that was it. They use the body and you get the cash (HV4).

> Whether you like it or not, money is the motivating factor for me, because if you do damage to your body the money plays an important role. Because they are doing something to your body, they need to pay, you know (HV10).

These participants understood that their involvement centred on an economic exchange: their bodies for money. That their bodies were being "used" denoted not simply a function but also exploitation for the purpose of obtaining results. For the volunteers, the "use" of their bodies would not be permitted without any compensation. The participants' experiences will be discussed under the following headings: healthy volunteering as a passive job, the body as resource and the dilemmas of market exchange.

Healthy volunteering as "passive" labour

For some participants, volunteering in clinical trials was just like doing any other job with terms similar to a contract or a quotation from a plumber: one is free to accept the quotation from the plumber who offers the best deal. This perception emerged in response to questions about how they saw the risks to their bodies and whether volunteering for a clinical trial was like selling their bodies. Both assumptions were seen as misplaced – doing trials was an economic exchange.

> … it's like calling a plumber or builder. You call out one, give the job description [and] they are going to give you all the details of what they do and price. Then if you are not happy, you go away. I have not actually known anyone feel that way [like a prostitute] but each job has risks you have to face (HV4).

Of interest here is how participants seemed to draw on daily discourses in which risk was seen to be an occupational affair and thus acceptable (Lyng 2009), and reference to selling their bodies prompted them to ask what was meant by "work"; their interpretation of healthy volunteering as being like any other work conveyed adequate motivational relevance for taking part. The participants questioned prevailing assumptions and expectations about employment – that "good work" involves working in an office or conforms to what society defines as a "normal job". In addition, as discussed in the literature review chapter, some forms of labour such as sex work attract forms of stigma as they are

seen as immoral or reckless work. For some participants in this research the general perception was that all forms of work involved selling one's body in the form of labour in that it involves the notion and reality of exchange as well as the use of the body, though in different ways.

> You know, people think being a volunteer is easy. That pisses me off a lot because it's really "hard work" [raises fingers to indicate inverted commas]. You have to put up with a lot of stuff, you know, like the needles and discomforts, and it's just demanding being woken up at odd hours. It's just like work, you know (HV4).

Clinical trials were seen to be easier and more rewarding than, say, working in Tesco; the challenge was to endure being kept indoors subject to strict rules and to give blood regularly.

> It's easy, you know [pause]. Accommodation is provided and they give you food and pay you for sitting around. So, yeah, it is hard work enduring the needles and all that stuff like bloods [giving blood]. But of course, it's better than working in a bar. You won't get paid that much (HV13).

> When you are blessed with good health you … you don't have that time or that resource to plough a mountain to be working really hard because you are busy doing other things and … you know here you just have to sit or lie on your bed and they pay you, better than stacking shelves in Tesco. It's not actual physical labour, it's more inactive, like (HV5).

It is from the participants' use of expressions such as "easy", "sitting or lying on your bed" or "not physically doing anything", yet earning money and creating value for the pharmaceutical industry, that I derive the term "passive labour". The term parallels Marx's concept of the production of value based on the exchange of objects for money rather than on relationships between people (Marx 1975). Though most volunteers acknowledged actively looking for clinical trials and doing that

entirely for the reward on offer, most of the participants regarded themselves, ironically, as experienced rather than as "professional" volunteers.

> Mwale: Would you describe yourself as a professional volunteer, then?
>
> P: What's the other option? If I am not professional, what am I? Um, not really. If I have to make more money I have to do more trials … I think I am experienced and realistic [about the] risks involved. Of course, the money is important but I think I look at the what [of what] they are asking of me (HV14).
>
> Mwale: So seeing the number of and frequency of your involvement in clinical trials, will it be fair to describe you as a professional healthy volunteer?
>
> P: Well, no not really. I am more experienced. I know what it takes and what is required. Yes, money is important but I am not running around looking for trials to make money. That's more like a professional, isn't it? Yes, money is what I do this for but not in that sense, I have a [day] job (HV4).

While it was clear that participants talked of doing clinical trials as a result of their socio-economic circumstances, they still wanted to be seen as principled and in control of their situations, they acknowledged the difficulties associated with the exchange entailed in clinical trials, such as the pain, emotional strain and powerlessness. The rules are set by the CRO, which has the power, and participants are reminded of it when they complain or raise issues.

> … You see, they tend to think … like, "We are paying you money and so why are you complaining?" So they do not pay attention to the things that we say. They would say things like, "This is not a five-star hotel and you are being paid to do this" (HV9).

The last extract reveals how pointedly the participants were put in their place, in a way that suggests bullying to ensure compliance.

Bodies as "resource"

The economic exchanges entailed in volunteering for clinical trials changed participants' views about their bodies. For some, the body became topical; it was no longer taken for granted but treated as a resource. This change was manifested in their efforts to improve their chances of enrolling in the trials and prolonging their participation in them to earn money. It was therefore motivationally relevant to see their bodies as machines that needed careful maintenance:

> … because I see my body as such, just in case I may need some part oiling, you know, and I wasn't aware of it (HV22).

> I am a healthy person, you know, I am not unwell. Doing trials has not changed anything … I know that you can't take this medication and they have side effects, and if they have long-term effects the body can recover and bring you back to where you [were before taking part in the clinical trials] (HV19).

These quotations bring to mind the concept of "biovalue" (Waldby 2002) in the ways in which the healthy volunteers worked on their own bodies to maintain their value in the context of clinical trials. Biovalue becomes explicit in relation to how the materiality of the body provides possibilities for both individuals and institutions to challenge prevailing ethical, sociological and legal understandings of the role of the body in medical research. Biovalue is linked to how prevailing socio-political economies of the body interact with social conditions to bring about certain forms of agency. Nor is it connected only to the biomedical developments from which it arises but also to socio-economic status and how this influences the individual's willingness or capacity to engage with risk. For healthy volunteers deep in debt, for instance, it is motivationally relevant to view their bodies as constituting biovalue with earning

potential. Many volunteers interviewed for this research saw their bodies as assets that needed to be maintained if they were to make money. They did regular exercise, ate less junk food and generally changed their lifestyles.

> I don't drink coffee or fizzy drinks. I make sure I eat a lot of fruit and veg and do a lot of exercise, and you know, keep the body free of illnesses, because if I do not get into these trials then I cannot earn the money. So I don't drink any alcohol and I don't take recreational drugs. I tried before in Romania, but you see, I have to look after myself. I think my body is valuable and I am lucky to have this body (HV 10).

> … we don't eat in KFC anymore. Maybe the first weeks we did, but now it's fresh produce. If we are not fit, they will not accept me at the trial. Then I lose a lot, so I have to do more exercise and so I don't eat burgers, Coca-Cola. We eat chicken or fish so we can buy from markets and negotiate prices (HV6).

> I have become more aware now of my health and somehow do pay [more] attention to my body than I did before. You know, when they turned me down it was like an awakening that I needed to change. I am happy to do the trials because I now have health checks and … it does help put things in perspective that the body is me, but much more, if I don't look after it well I cannot make the money that I need, so yeah, my body, I must look after it well (HV4).

It is noteworthy that the body becomes topically and motivationally relevant, to use Schutz's (1970) concept, as "capital", often after the individual is turned down for a clinical trial because he or she is not fit. The rejection made the body interpretively relevant; volunteers started to think about their bodies differently, which triggered lifestyles changes in order to make their bodies "marketable" for exchange in clinical trials.

The body is topically and motivationally relevant as a valuable resource not only to the pharmaceutical companies; it is equally so to the

individual who embodies and offers it for exchange. But notice the contradiction: while the volunteers took greater care of their bodies through diet and exercise, for instance, taking part in a trial put their bodies at greater risk. The participants seemed to draw on discourses of risk in everyday life to interpret or explain what they were getting into. These complexities are explored in details in the following section.

Exchanging the body for the reward in clinical trials

While money was motivationally relevant, it also shaped and perhaps even distorted the experiences and views of participants in the trials. Due to the monetary reward on offer the participants lowered their guard against risks and resigned themselves to situations they would otherwise have challenged:

> Money was very important for me. I wouldn't go in there for free, you know. I just need the money, but what happens with the money issues is that it changes your experience and maybe your expectations … you start to put up with people not being nice, or if things go wrong you start thinking there must be a rational reason why they are doing this (HV29).

> I think the first trial I did, I was very careful, but from the second onwards … money also played a part in making me stop worrying about the whole process (HV5).

In addition, being paid also seemed to influence the participants' topical and interpretational relevance of adverse effects or to generally having a negative experience on the trial. Some participants interpreted the payment as a reward for coping with being confined indoors for long periods. Others felt they had no choice but to endure the hardships.

> Money was very important and you cannot deny that, because as you do these things you meet all sorts of people who show you around things and remind you to focus on the money … They [staff] also explain it to

> you: "It's just simple, we take a bit of blood and a bit of some examination here and there, and then you get the money." This looks very straightforward, but it's hard (HV9).

One participant observed that the exchange evoked feelings of physical vulnerability and powerlessness:

> I thought about that for a while. I think volunteering is a kind of violation of your body and you can't really separate it from your body … because that's just me, you know, part of me (HV5).

> Your body is who you are, and as a result, you may become very sensitive, just like this woman [a volunteer who became ill as a result of the food] may have become upset about it [the trial process]. But there are worse jobs to do for money (HV29).

The participants seemed to find themselves in a conflict between their decisions to become subjects of the trial and allowing things to be done to their bodies for reward while struggling to come to terms with the hardships they had to endure. At this point they seemed to view their bodies as closely linked to their identity. Participants spoke of how they started to redefine their bodies as "who you are", a self-image that can be detached from one's sense and experience of oneself. Though the participants were aware that they were involved in some kind of exchange, part of their struggle seemed to come from contending with the idea of selling something and giving it up completely, and the idea of selling something and yet still possessing it, in a sense (they gave up their bodies for research and yet were still embodied beings with a strong sense of physical embodiment). In everyday life once items are sold and have new owners, their original or first owner no longer has any say over what happens to those items, no matter how much they might have meant to them. However, with the body in clinical trials, they retained a sense of owning their bodies in a form of "passive labour" – the concept I introduced in the previous section – in that while manual labourers put

their bodies to work, volunteers in clinical trials see their bodies worked upon as they sit and observe the process. At this juncture, ethics of volunteering come into play as conflicts associated with rights emerge: when does the body in such transactions lose its private dimension and become "public" or even "corporate"? While ethical debates mobilise the discourse of "ownership" and/or "property" with regard to individuals' bodies in clinical trials, the topical and interpretive relevance for most volunteers in clinical trial transactions is to do with the loss of control over their bodies. They have the right to withdraw from a trial, but pulling out can have serious consequences.

> It's all very uncomfortable, erm … very invasive. You know, like the doctors can pick you up, put a needle in you, take your blood and do what they want with you. And you have to comply, because you signed a consent form at the beginning which says you will comply. I mean, obviously you can walk out, but then you lose everything. Like I, erm, withdrew myself from the trial. Later I didn't receive any compensation for the five days that I did, nothing… (HV5).

The above quote illustrates the complex nature of the role of the body in clinical trials. Doing clinical trials for these participants involved complicated negotiations over power relations. In addition to exchanging the body for money, participants also found that in giving their bodies for research they inevitably gave up control and power over their bodies as they were reduced to objects from which data could be obtained. Although the process is subject to regulation, the exchange is weighted in favour of the research companies – they have the power to set the terms of the exchange.

For some participants the loss of power, vulnerability and hardship made them feel that they were engaged in a kind of prostitution.

> … but after the first one I had this strange feeling, you know, I felt like a prostitute, because I was feeling like I

> was using my body, because I felt I was giving my body to someone in exchange for money (HV9).

Such feelings often evoked guilt, a questioning of the "right" way to make a living, and were a deterrent for some; others came to terms with it. Feelings of vulnerability prompted one participant to reflect on issues of identity and the meaning of work. Making her body available for clinical trials was at odds with her job as a model and actor, for which the body is equally central in the exchange, although in a different way. What was most topically relevant for her, however, was the loss of power and control during the clinical trial.

> I also did have this little disturbing feeling, considering what I do for a living. I felt like I was sinking low and cheap, like I am going in there, sign off things, take a drug and give my blood, you know, like using my body like a prostitute. Like really, how cheap am I? Is this what it takes to hire yourself out like that? Then I sort of started to get myself out of that feeling by thinking of how useful my actions were in someone's life at some other point. It wasn't just for me and the money, if that makes sense. But living in London as a girl and working in the show business, that kind of work, you tend to sell yourself, so you kind of get used to that. But it was so strange for me to feel that way when I did the clinical trial. But obviously here there is a lot of control that you give away wilfully, you know, and that's what made this whole experience even worse. Yet despite all that, you sign up for it because you think, here is something I could do to make some money easily and still help someone else (HV 12).

However, for other participants comparing healthy volunteering to prostitution was taking the challenges of clinical trials too far. They compared healthy volunteering with work in other settings and argued that participating in a trial was not comparable.

Others rejected the comparison with prostitution. While acknowledging how topically relevant (Schutz 1970) the issues they faced

in clinical trials were, and how they could be associated with prostitution, they saw healthy volunteering as a personal choice and believed they knew what was being asked of them. Others compared healthy volunteering with any conventional work. Besides, prostitution was beset with gender politics.

> So I didn't feel that way [like a prostitute] about myself at all, but I can see how and why they felt that way … And it's part of the things you sign up for and I am aware of what is being used of me, and I am aware of what I am taking away from them. So I was equally aware of the fact that it's some kind of a transaction … I mean it's not a sexual power domination. It's not domination because I am sitting there and interacting with other female doctors and female nurses. There is an invasion of my body, but it's nowhere near that which happens in prostitution, you know. That is about power and control, and the interaction I am having is about resources, money and knowledge. I mean there is power in some way in that you are made to [finish] your food, when you sleep and when you wake, and just when they want to do what they want to do in terms of schedule procedures, but is nothing in comparison to what happens in prostitution. On that level then, they are not comparable, on the level that my body can be used for, then, yeah, but for me I think we have to be careful about that comparison. The sexuality thing is about the value of oneself and goes deeper for me (HV29).

> [laughs] No, absolutely not. For me this is a transaction. They know what they are getting from me and I know what I will be getting from them. I understand the similarities [between prostitution and healthy volunteering] in that people resolve to do trials due to their economic issues they face, which is the same as in prostitution, but for me it's like any other work. People, we use our bodies, don't we? HV4.

Most of the participants who spoke of healthy volunteering in positive terms had not experienced unexpected side effects while taking

part in clinical trials. They had explanations for the side effects that did occur, and often seemed to accept them simply as occupational risks (Lyng 2009). The risks and loss of power were therefore not as topically relevant for them as for other volunteers. However, those who invoked the comparison with prostitution had all experienced unexpected side effects, making risks and powerlessness topically relevant and consequently requiring an interpretation. The experiences changed their perception of clinical trials.

The economic exchange entailed in healthy volunteering changes the perception of work and the body. The changes give rise to dilemmas associated with the relationship between institutions, market exchanges and the body. The interview data demonstrate the limitation of the free market exchange model when applied to healthy volunteering in clinical trials. The model is problematic in that there are major power differences at play in the transactions. While participants were clearly aware of the nature of the exchange in which they were engaged and their rights, it is undeniable that professionals and institutions wield the definitive power to control the terms of the exchange and to shape the nature of the exchange itself. The following section considers healthy volunteer accounts of voluntarism.

6.4 From market exchange to gift relationship?

In the literature review chapter, I discussed the gift relationship (TGR), a concept drawn from Richard Titmuss's ground-breaking work on altruism. The gift of blood in regard to blood donations has fuelled debates in social policy about the nature of our interdependence as a society. TGF has been widely used in sociological discussions on the role of human involvement in medical research such as genetics (Tutton 2002), organ donations (Nuffield Report 2011) and research involving patients as volunteers (Hallowell et al. 2010). The concept is used as a point of reference in discussions about the moral significance of charity and the act of giving when nothing is expected in return. More recently, the concept has been applied to donations of body parts, while tissue banks are viewed as a public good (Waldby and Mitchell 2006; Waldby 2006; Axler et al.

2008). This section explores how healthy volunteering can be understood as a form of TGR. I also analyse the relationships between volunteer research participants and research teams in CROs.

A few of the participants in this study gave accounts of volunteering free of payment. They first became involved because they were in financial difficulty, and continued to volunteer when they no longer needed the money. For these individuals, volunteering became a gift relationship.

> … well, depends really. One unit was particularly good to me, you see, when I was in a sticky situation. So I think if they urgently needed me, I can see what I can do. [It] also depends on my time and work schedule (HV9).

> … it depends. Some researchers are good and they were good to me, so if they are doing a study and they said to me, "We have little money, we can't pay you." I know them. I would say, "Yes, I will help you", because they helped me when I had a bad time. They ask you, call you by name and make sure you're okay (HV16).

These accounts are in sharp contrast to the preceding quotations about economic exchange and unequal power in which participants spoke of feeling exploited. The above accounts illustrate how power works in subtle ways – rather than overtly coercing participants, making them feel special made them want to come back to "help". Most participants continued to volunteer after their financial situations had improved. The positive change in their circumstances brought about a change in their attitude to volunteering. A small minority volunteered again as a way of thanking the research team that had admitted them to a clinical trial; reciprocity became the motivation. Some participants seemed to feel indebted to the research team for having been "helped" when they were in financial difficulty. Research teams could be seen as deliberately fostering such feelings.

> They call me and have often told me I am a model volunteer, and they often call me first when they have a new clinical trial and they start recruiting. So I am among the first to know about this [giggles] (HV1).

Such feelings of loyalty or willingness to cooperate affected how the participants interpreted follow-up calls from the CRO's recruitment teams who checked on their wellbeing after they had completed a trial. Participants who were invited for another trial were more likely to commit to repeated participation, and some started to think of themselves differently. An invitation to volunteer was seen to come from a trustworthy and caring professional who had their best interest at heart. At this point, lay sources of information were less likely to be used and participants were less likely to research the drugs they would test. In making the participants feel wanted and appreciated, the research team were able to influence the participants' views about volunteering. Some participants talked of the researchers as "being good to me". This demonstrates how the relationship between volunteers and researchers changed from an economic exchange to a gift exchange. It also demonstrates the subtle ways in which relevances – topical or motivational – may be imposed by institutions or powerful figures to influence individual agency.

> I would say that money is not as important as it was before. It depends on how much they would require of me. If it was a day or two or a couple of hours here or there, it is not too bad. I mean for me, at the moment I only have Fridays off from work, so I can't actually take time off to do it. So if they want it to be over a long period of time I would not be able to do it, but if they want to do a couple of hours – Mondays, Wednesdays and Fridays – I would say okay then. So yeah, I would do it as a one-off, but I don't think [I would] do more [giggles]) … more than one, you know. It's time (HV1).

> … sometimes it depends. If it's a unit where I had good rapport with staff and I have time and they called me for trial and they are offering little or nothing for a short study, I would say,

> "Yes, I can help", because basically they were there for me when I needed help, really (HV10).

It seemed that the participants interpreted an affirmation of their suitability for the trials as a sign that the research team cared about them, highlighting the complex interplay between the notion of the gift, gratitude and altruism.

> … they have called me a few times and actually they have told me I am good and reliable, so I am among the first people they always call to check if I am available for a trial. So it's a good relationship (HV1).

Doing clinical trials was seen as a moral obligation by some. They viewed volunteering as giving without expecting a return. A few participants cited personal beliefs, for example, their opposition the use of animals in developing drugs.

> … yes, because I don't really need the money. In fact, I did it because I am against animal testing [for drugs for humans]. So I thought, if I oppose that then I better just do it myself (HV 12).

> … yes, I can do it for free if somebody asked me to. I mean, my goal is to help people. The money is good, but … someone has to give some[thing] to another without expecting something back. It's my duty, I think, to help (HV15).

The declared willingness of these participants to volunteer without expecting anything in return challenges the concept of the gift relationship. For Titmuss (1979), TGR should be based on mutual benefit. The views of these participants, however, seem to be more in keeping with ideas of biological citizenship, biovalue (Waldby 2002) and social responsibility, as discussed in Chapter 2, in accordance with which individuals are expected to give something back to society. Those who held such views were in a distinct minority. Most of the others laughed at the idea of volunteering without being paid; some even questioned the sincerity of those who claimed to be volunteering for the good of society.

6.5 Summary

This chapter explored the complex nature of the exchanges that take place in clinical trials. In Chapter 2, I had discussed the ways in which the role of human participants, especially healthy volunteers, has evolved since the 1970s and how neoliberal ideology has influenced the way the human body is viewed. In examining the economic dimension of the exchange in clinical trials, the chapter showed how healthy volunteers entering clinical trials found themselves negotiating a process of commodification, which included experiences of depersonalisation and institutionalisation. Participants were generally well aware of the nature of the exchange, the power relations involved and the cost, both psychological and physical, of their involvement. They had to come to terms with the idea of having to sell their bodies and were subject to pain and emotional distress during the trials.

Healthy volunteering was shown to shift from being a market exchange to a gift exchange, and was seen by some individuals to be a social responsibility. For others the economic exchange was reciprocal, involving a sense of connection with the researchers or of a favour owed. In analysing the participants' experiences this way, the chapter demonstrated the ways in which relevances may be imposed by institutions and those in positions of power. Most rejected the idea of volunteering for altruistic reasons; rather, they argued, it was purely a market exchange and it was the financial reward that motivated individuals to get involved in clinical trials. They tended to dismiss assertions by a minority of their colleagues that they felt an obligation to volunteer for the good of society. Nevertheless, the idea of a "gift" did occur among some participants in this research. Accounts of economic and gift exchanges in healthy volunteering in this chapter invoke the notion of biological citizenship (Rose and Novas 2004; Petryna 2009). Using Schutz's (1970) system of relevances the chapter has also shown how the contexts in which individuals find themselves influence their decisions and behaviour as well their interpretive understanding of the institutional structures and inequalities they engage with. Here it was suggested that the body itself

acquires 'topical relevance' in Schutz's terms, as a resource for making a living by taking part in clinical trials. The following chapter considers the interaction of risk and trust in clinical trials.

Chapter 7
Risk Strategies, Trust and Constructions of Rational Consent

7.0 Introduction

Most debates about the role of healthy volunteers in clinical trials in relation to risk focus on volunteers' management of risk, their capacity for rational action, and individual liberties. Most bioethical and socio-economic understandings of individuals draw on rationalism as the guiding principle of human thought and action (Hale 2007; Hayden et al. 2007; Montgomerie and Williams 2009). This view is prevalent within behavioural economics and widely held in society at large. Bioethicists and behavioural economists argue that people are capable of demonstrating "complete" rationality, with faultless recollection, and of forecasting alternatives and consequences based on their decisions to maximise value in a complex world of interactions and exchanges (Lewis 2010). They see the key to helping people acquire this capacity as the provision of adequate information. This perception is influential in our understanding voluntary engagement with risk in clinical trials. Corrigan (2003) suggests that policy solutions and debates about risk in volunteering for clinical trials are based on the idea of individuals as rational actors who are well informed and fully understand the contracts they sign.

Individuals in the West have come to understand themselves and their experiences in terms of the outcomes of their own actions and the rational decisions they are supposedly capable of making (Gill, 2008; Layton, 2010; Walker at el 2013); they are perceived as being autonomous, rational and creative. The same view is held of volunteers in clinical trials, who are assumed to be informed, knowing actors who willingly put their health and even their lives at risk, rather than subjects of a complex and problematic socio-economic system.

This chapter critically examines the relationship of monetary rewards and risk in the informed consent process and the concept of healthy volunteers as rational actors. The role of trust and its application in

healthy volunteer engagements with risk is also considered. While professionals may see risks as objective and volunteers as informed rational actors, the volunteers' idea of risk is shaped by their often complex social circumstances (Schutz 1970). Information given to volunteers during the admission and consent process is shown to be not always of topical or interpretational relevance to volunteers when they decide whether or not to take part in a clinical trial. Volunteers vacillate between trust and mistrust in their negotiation of risk. This is further affected by the relationships with others in and outside the clinical trials and by the healthy volunteers' financial circumstances. The chapter demonstrates that in order to better understand healthy volunteering and to improve the informed consent process, wider social economic issues need to be taken into account.

7.1 Professional views of healthy volunteer conceptions of risks and rewards

Accounts of individuals as rational actors in relation to their understanding of the risks involved in FIHCTs emerged frequently in the data gathered for this research. It was clear that the professionals believed that applicants and volunteers were well informed and fully aware of the risks involved in clinical trials; the volunteers were therefore personally responsible for the decision to take part in clinical trials and for any failures to understand the risks involved. Professionals found it difficult to understand why volunteers would complain about the pain, discomfort or risks involved in clinical trials:

> No one is forced to enrol into a clinical trial. People decide to do it and they understand the risks involved (Corporate Professional 2).

> … Well, information is made available and they use that to decide to take part so they understand what is involved in the trial. No one would complain about that [risks] (Corporate Professional 3).

Professionals believed that volunteers had a misplaced view that the money offered for participation was commensurate with the risks involved in clinical trials; the money was meant to compensate volunteers for their time and discomfort, but not for any risks.

> Mwale: Why do think volunteers think that way about risk and payments?
>
> P: Erm, I am not sure, your guess is as good as mine … why would they be paid so well if it wasn't dangerous? I think that's one of the things, if you pay them so well they think that it must be dangerous [clears throat]. In fact, we pay people for turning up and the inconvenience and [coughs] discomfort, but we, we are not allowed to give them danger money. And if we were giving them danger money, we wouldn't be erm, erm … that means that the study isn't safe and so we wouldn't be doing it. But, erm … many of the volunteers don't really see that; they think that these things, they don't realise perhaps that the studies are as safe as they really are (Corporate Professional 1).

According to the professional view, when volunteers took issue with the risks involved in clinical trials, they focused too closely on the monetary reward. Corporate professionals do not see the payments as inducements and therefore inherently problematic in wider socio-political and economic terms, and they are thus not topically relevant. Engagement with risk is perceived in terms of individual responsibility rather than the result of broader societal factors. Professionals seem to have adopted an idealised, abstract and procedural (Douglas 1987) view of healthy volunteers.

7.2 Informed consent and monetary rewards

The literature reviewed for this thesis highlights that provision of adequate information is central to the view of individuals as rational actors (Scocoza 1989; Corrigan 2003). Bioethicists see this as the answer to ethical problems that may arise from human involvement in clinical trials,

but recent policy and academic debates about volunteering in clinical trials point to the inadequacy of information for participants about the inherent risks (Corrigan 2003; Fisher 2007). There is emphasis on increasing awareness and ensuring that individuals are capable of taking responsibility for their own decisions to participate in clinical trials (see for instance Paragraph 3(1) of Part 1 of Schedule 1 of the Medicines for Human Use [clinical trials 2004]). The view is that information not only makes issues of risk "topical" to participants but that it also helps them in making decisions.

The view that the provision of adequate information is the solution to ethical challenges in FIHCTs is also reflected in the development of regulatory measures. The 2004 Medicines for Humans Regulation is explicit about excluding individuals considered incapable of making informed decisions by virtue of physical or mental problems. The regulation makes the following provisions:

> (i) Providing information to potential subjects, including a contact point where additional information can be obtained about the trial and the rights of trial subjects,
>
> (ii) Providing subjects with updated information during and (where relevant) after the trial, and
>
> (iii) Obtaining informed consent (The Medicines for Human Use [Clinical Trials] Regulations 2004).

The professional participants in my research generally believed that ethical problems associated with risks in clinical trials and over-volunteering could be resolved by educating volunteers:

> Our consent forms are between 11 and 15 pages. So they get a lot of information about the medicines and the study which they read. It's usually distributed to them or sent to them before the study via e-mail or ordinary mail before they attend the screening, and so when they come for screening, they see a doctor, they ask questions and the doctor tells them a bit more about

> the study maybe, and they sign a consent form (Corporate Professional 2).

> Let me start by saying that our existing systems of dealing with problems like these are actually better now than before, and while there is always room for improvement, I think there is nothing more that we can do. Participants are provided with information and there are measures in place to follow these through. For the participants in this research there was a general satisfaction with the existing systems of obtaining informed consent (Corporate Professional 1).

There seemed to be a reluctance on the part of the professionals in this research to consider the role of rewards and the wider socio-economic and political factors in shaping volunteers' perception of and engagement with risk in clinical trials. In the aftermath of the 2006 Northwick Park cancer drug trial, in which several healthy volunteers suffered unexpected and life-changing side effects, the immediate policy response focused on the need to review safety systems. The government inquiry was silent on monetary inducements and what role they may have played in the trial.

For the professionals in this study, the individuals involved in clinical trials were informed and capable people, but they generally failed to take into account how socio-economic circumstances, such as excessive debts and loss of jobs, can make individuals vulnerable to exploitation (Mandeville 2006; Morris and Bàlmer 2006). The professional view of rational actors is based on mental capacity, which is based on an imaginary "rational actor", rather than how wider socio-political circumstances and personal financial needs can distort people's concepts and perceptions of risks. As a result, within this discourse people who do not fit the set criteria of vulnerable individuals are often construed as "capable individuals" to give rational consent. This is a simplistic conclusion and one which does not take into account other dimensions of vulnerability which do not relate strictly to physical or mental illness. When individuals are desperate for money, their knowledge of the risks involved in clinical trials becomes irrelevant. While the professionals generally seemed aware that monetary

reward attracts people from disadvantaged backgrounds or in temporary employment to take part in clinical trials, they saw this to be a normal part of the business.

> Obviously, this [issue of monetary rewards] is an issue that I think everyone is aware of with regard to coercion, but I can't do anything about it. I can't say to people, "No, you can't do this because you don't have money or you are poor so to speak (Corporate Professional 1).

In the above extract it is also clear that professionals are aware that payments put pressure on participants to take part in clinical trials. However, among the limitations to the idea that information provision resolves all potential ethical problems is not just that it is topical to people in desperate financial situations, but also that efforts to inform participants of the risks are contradicted by the interests of or rather issues of topical and motivational relevance (Schutz 1970), of certain organisations involved in the business of clinical trials such as the pharmaceutical companies, CROs and governments.

CROs pride themselves on their proficiency in recruiting and retaining participants. Information about risks might therefore be presented in a way that does not make risks of topical relevance to potential volunteers. To remain competitive requires that CROs offer better incentives to volunteers. Individuals in straitened circumstances may therefore overlook vital information when considering the attractive rewards on offer. That ethics committee members are aware of this anomaly can be seen in this extract:

> So if someone is going to offer participants, say, £20,000 and we know that they are targeting predominantly an unemployed, out-of-work population, because that's what they want to study, then we could have concerns. That amount of money would be way more than [they] would be able to get in a year and it might blinker them ethically. It might be coercive to

> make them look at the money [rather] than the small print … and that's what we would raise as an ethical issue. So, yeah, money on offer is an issue for certain groups (REC Official 10).

The professionals sampled in this research had two attitudes about the role of information. There were those – mostly industry representatives and corporate professionals – who felt that it was the only course of action available in terms of alerting volunteers to risk and that the system was adequate in dealing with any ethical concerns that might arise in practice. The problem here is that it clearly (if subconsciously) draws on the concept of individuals as rational actors; as people who are able to make "informed decisions". Therefore engaging with risk in these trials is construed to be an individual's responsibility that could only be addressed or alleviated with more information. The others, who were mainly REC officials, agreed that providing adequate information was a solution to the problems of risk but they argued that more needed to be done to improve practices and regulation in clinical trials in order to better protect volunteers from undue risk. They were sceptical about the effectiveness of the existing approach as there were no means of monitoring the sharing of information that follows recruitment in clinical trials:

> Mwale: But … how do you know that volunteers are informed as outlined in the information submitted to the committee for review?

> P: … we don't have anything or any system or any documentation or record that shows me what happens during the consent process of a trial. What we have is a sheet with tick boxes that [show] the patient has understood what it is, but actually if you want your money you will tick those boxes regardless, which is why we have no record of what the patient person actually… understands [in terms of] what the study is involved with [in] regard to risks and benefits. Which is why I think we should have a patient's own verbal record of what they think they understand the study to

> be about, and what … they think they are actually signing up for (REC official 9).
>
> Mwale: So how do you make sure this information is communicated as outlined in the protocol?
>
> P: So we look through the papers and see that information is clear and that it is in lay language. But how this is done in practice is obviously not something that we monitor. Sometimes the information is good but other times it's not clear and we have to ask for them to change [it]. But I also see what you are trying to say – [that] we need to monitor how consent is obtained and whether participants decide after information is given or not. But we don't do that (REC official 10).

These REC participants in response to prompting clearly felt that more needs to be done to address the issue and possibly improve ways in which information is given to participants, including subsequent monitoring of how they understood the information. Given the context in which decisions are made and the individual's financial circumstances at the time of deciding to take part in clinical trials, it is difficult to take the view that such decisions are always purely and simply a matter of making a "well-informed choice". There is no clear agreement on the impact of provision of information on people's understanding of risks, not least because the matter has not been well studied in reference to healthy subjects' involvement in clinical trials. Improving awareness does not result in better practices, attitudes and behaviours among healthy volunteers, because the provision of adequate information does not solve the financial problems they may have (Kamleitner et al. 2012; Mitchell and Mickel 1999; Watson 2003).

7.3 Engaging with risk in healthy volunteer clinical trials as a norm

As outlined in Chapter 5, taking part in clinical trials takes different forms. In terms of demographics, it is not just the young and unemployed who volunteer for such trials. Rather, as I have shown, participants come

from a variety of backgrounds and socio-economic circumstances. The number of clinical trials that take place in the UK is also indicative of how widespread healthy volunteering in FIHCTs has become. Taking part in clinical trials has for some become a habitual and rewarding practice (Lyng 2009). While they may be driven by factors such as debt and unemployment (Lupton 1999), healthy volunteers in this study felt that engaging with risk had become normal for them.

> If I worked over the summer or work during term time I will work in a bar to raise money for fees and accommodation … To make 1500 quid in London, it is impossible, or I mean it would have to be a nice bar, and you have to work fucking hard … Whereas, if you compare to … volunteering in a clinical trial for a week, I earn more than what I would get if I worked, you see. So I am able to pay uni fees, travel around the city and pay my rent (HV5).

> You know, it is normal now to do things like this. You know, people I meet on the trials like me are graduates with professional postgraduate degrees. Ten years ago, I would have had a job, a house, a good car etc., but now it's impossible. That is just a dream. You have no job, nowhere to live, maybe going back to live with your parents, but who wants that? All you can do is low-paid temping jobs. So I am left with no choice but do this [being a healthy volunteer] (HV25).

The participants were generally well aware of the stigma they attracted by taking part in clinical trials, but felt that managing and engaging with risk in this context had become normal (Peretti-Watel and Moatti 2006). What was of topical relevance was the prospect of failing to manage and negotiate the risks and the possibility of being seen by their immediate families as struggling financially. Such failure was seen to be to a source of shame. There was a tendency to look down upon fellow volunteers who focused too much on the monetary rewards, who ignored risks by taking part in trials indiscriminately and on a regular basis,

especially if individuals persistently take part in very FIHCTs. Some saw this as a failure of personal responsibility:

> I was a little bit, well, I found it quite strange to be in that environment, but what was really strange is that I felt like a novice. Some people are really used to doing this and they do not see the problems that I saw. They seem to be coming regularly for trials, something which was quite unnerving for me. They are willing to do any trial regardless of the risks. It's worrying because someone needs to think about the implications for this … It's absurd (HV12).

> For me it was about reading the information and making sure I know what I am getting myself into. It's shameful because [for] a lot of the people I have seen, it's about the money and they pay no attention to the risks … they see how much they were going to get and they say, "Oh, yeah, I am going to do that one". I think, yes, money does sway people's perception of risks in these trials. It is interesting that people will do everything for money and sometimes people will take risks that they will not necessarily take if they will get a financial reward for it (HV19).

Family members of most participants did not see clinical trials as an honourable way to make money; rather, it was taken as a sign of struggling financially and therefore a source of concern. Some decided to keep the matter to themselves.

> I decided not to tell them [the family] because they tended to be very worried about me. My brother said that I was putting money over safety, that I love money too much; why am I putting my life at risk? So I didn't want them to worry, so I decided not to tell them, though my wife knows about it and she is very supportive (HV9).

> My mum said, "Don't be stupid, it's a silly idea. It's reckless. You will make yourself ill and there is no need

> for you to do that". I tried explaining that it was safe but they said … in a way there was an undertone that I should do something productive with my time [rather] than getting myself involved in clinical trials. "Get a job or something," she said (HV22).

A major concern was to avoid being seen as reckless or as a "professional healthy volunteer". Being a "professional volunteer" (Abadie 2010), as discussed in the literature review, was associated with being reckless and greedy. This seems ironic; in a society influenced by libertarian concepts of the individual in which individual choice and liberties are accentuated, it seems that living up to wider societal expectations is still very important; while still motivated by the monetary rewards (Schutz 1970), the volunteers were very keen to avoid being stigmatised. The concern over being stigmatised (Bendelow France and Williams 1996; and Peretti-Watel et al. 2007) also seemed to shape or influence the participants' response to questions about risk.

> Yeah, I told them [the family] once. They were a little bit afraid for me; they did not have a lot the facts. I think they just heard it's a trial and they were scared. My dad asked me to go back home if I was having problems with money. He will look after me, he said. Well, so, after some explanation, I was able to convince them and they reluctantly kind of okayed it [taking part in a trial] but still they are concerned [HV6].

> Mentally I was younger, so I suppose it was like a jolly boys' outing, really. I did not talk to a lot of people about it initially because they are not enthusiastic about me doing this. Because when I started, they would try to put me off. At the end of the day, it's your life. Probably just one to two close friends and obviously [there were] some mixed reactions. And so I don't want them to be worried about me so I kept it to myself. Mentally I would just close in, really [during] maybe a week in a hospital or in a unit (HV5).

Other volunteers felt they were failing to meet expected income standards and had to do clinical trials to make a living. Most decided to take part in the clinical trials upon seeing the advertisement, but mainly because of the money on offer; the information provided at admission or received before the trial was rarely of topical relevance. Most went through the admissions process by which point information had already been given and a decision to participate had already been made.

> I do often have the information needed, but you see, when you are in dire need of money, food and fees and all that stuff … It's no need to tell me about the risks involved, you see. I want the money … that's all I want and I can't run away from it. It's like being [between] a rock and a hard place (HV 5).

Such statements highlight the limitations of the informed consent process. Clearly, being seen to be able to make informed decisions and being provided with information does not mean that individuals are making informed decisions. Participants generally responded to risk in two ways: those who saw the risks involved in clinical trials as inevitable and as comparable to any other risks in life, and those who saw risks as an imminent danger to be avoided.

> … but even as you walk in the streets you are taking risks and inhaling toxins and smoke and you may even get hit by a car but you have to trust that that will not happen to you (HV2).

> Well, you know, life is all about risks, even making soup in the kitchen is risky, and so [you] cannot be sure what will happen next. So that is the same with taking part in clinical trials. So every day is risky, even crossing the road is. So I am not nervous about it. So what we do is keep healthy and live a happy life (HV6).

> Mwale: What about the risks involved in clinical trials – how do you deal with that?

> P: Well yes, there are risks, but so is life in general, one has to do what they have to do in life to make ends meet, you know, so it don't worry me at all. Yes, I do think about "what ifs" [what if a trial goes wrong] but I do that in most things in my life (HV11).

> … I was absolutely fine with that. But I don't know whether it's because it's to do with youth and, you know, this kind of feeling of infallibility and invincibility. And also believing that nothing bad will ever happen to you. You will always be fine … and you do see things as normal, you know, because they are there in all parts of your life (HV5).

For these participants, being of a relatively young age they felt they were thus willing to engage with risk regardless of the potential outcomes, which they did not investigate too closely. As outlined in Chapter 5, questions about their motivations for engaging with risk made participants reflect on their decision to take part in clinical trials. Of significance here is how participants draw on everyday discourses when talking about their decisions for engaging with risk. The participants saw risk as something they engage with in everyday life; hence there was no difference between risk on the streets and risk in trials. Others used age discursively as the precursor of their involvement in clinical trials. It was common for participants to decide to become involved before examining the information about the trial.

> … I must honestly say it was pretty much when you see the adverts before I went to the screening. I looked at the money and looked at the work schedule, thought I could fit it around work and decided right away … I decided way before the screening that I am going for this unless they do not put me in because of tests. The first one, I was a bit cautious. I decided at the screening. Because the first time I was not sure what to expect and after that it became easy. I knew what they wanted. So I decided to do this regardless (HV4).

> … You know, I also have to look at the fees and the time. Then I decide. By the time I go for checks I have already decided, I must say. I also looked at the details … and use that to make my decision. Once I have decided I don't normally have second thoughts. Like right now, I have turned down some calls because I was too busy in the past. So yeah, I decided the times I saw the advert and did not go back on that (HV2).

The prospect of monetary reward was often seen as encouragement in coping with the stresses, and pain and other problems they encountered in clinic trials.

7.4 Trust and past experiences

Some participants took part in clinical trials whether or not they had adequate information. The Nuffield Report (2011) states that central to good regulation and practice of research is the need for transparency; it is key in establishing the trust so necessary for individuals to volunteer for research. They are considered more likely to volunteer "if they are able to trust in the integrity, not only of the individual professionals involved, but in the organisational systems" that are required to ensure their safety, that their rights are protected and that the research will be appropriately conducted (Nuffield Report 2011). Some of the healthy volunteers interviewed in the study stated that their continued involvement in clinical trials was based on their past experiences of clinical trials.

> … there are certain factors that determine your involvement, you know. It's your past experience, level of monetary reward, how long you are staying in for and whether your work schedule would allow, and on the par with money is the facilities and how good the facilities [are] (HV4).

Adverse experiences such as a trial going wrong or unexpected side effects often made participants suspicious of professional knowledge and expertise.

> [After experiencing unexpected side effects]. It makes me lose confidence in the trial maker's ability to know everything about the drug and its effects, and I do not trust them fully after this. I am becoming cynical. There is a limit to what they can know or predict and that makes me more hesitant (HV 25).

On the contrary, incident-free clinical trials tended to lead to repeat volunteering.

> … but what was more interesting about the third one that I did, 'cause the second one I did no research for at all… I actually did the one in September and I did not do much research on what the drug was (HV5).

> I did some research on the drug before I got on to the first trial … but for the second one, the one which was cancelled, I did not even bother. The third again I didn't bother. I thought it was going to be fine. But … the mental preparation when it came to staying in hospital for five days and all what it meant, I did not anticipate that (HV3).

Previous experiences seemed to make participants comfortable with the risks. Some began to believe that the system was actually working. As shown in the quotations directly above, participants who had experienced no side effects in previous clinical trials generally had more trust in the system and did less research on the drugs that would be tested on them. This is interesting as it shows the complex nature of trust in operation in the professional and lay interactions (Walls et al. 2004). If things are going well people are likely to put their guard down and postulate that things will continue to go well. In addition, in this study it was seen that using past experiences as a measure of what was to come could lead to an escalation in the type of clinical trials in which participants took part. Some decided to volunteer even for studies which they claimed they would previously have shunned. For these participants risk seemed to diminish or become less relevant in the decision making process (Peretti-

Watel and Moatti 2006). In other words if participants had no unexpected side effects, risk was not topically relevant (Schutz 1970).

> You start to think, because the people doing it [conducting the clinical trial] are professionals, and then you know they can be trusted, you know, to do their job right … then I am more likely to do it again and worry less. I trust that they know what needs to be done (HV5).

As discussed in Chapter 2 (Lash 1993; Tullock and Lupton 2003), the professional backgrounds of some participants – medical students, nurses and medical biological scientists, for instance – seemed to contour their views of and responses to risk and trust in clinical trials. They had an understanding of what the process entailed and generally had no problem trusting professionals to do their jobs.

> I have worked in research within medical settings. It means that I view the clinical trial itself differently, you know. I am more likely to do it because I know what needs to be done and I understand the language. I know how research is conducted and it's easy to understand the processes and that dropping out of the trial is not good for the data (HV15).

> I know what goes into preparing for a trial. I understand what they will be doing and the value to society of what they are doing, and the consequences of having good participants (HV19).

Their professional backgrounds also seemed to shape their responses to adverse effects during the trials. They understood the significance of the data and the implications of dropping out of the research. As a result, they often downplayed their experiences of side effects and were more inclined to persevere in the trials.

> I was very lucky. I only developed a blood clot at the last day and it was only a 12 cm one, which within 24

> hours was down to 3 cm. So yeah, I was, like, very, very lucky but I was very aware of what was going on. … Erm, I did panic a bit but at the same time I was, like, it was the last day of dosing … I know some had, like, five or six blood clots, and really big, so yeah, but the progress made me feel better, but the clots were on the sites of the cannula stretching upwards, and everyone was panicking, saying if it moves to your heart or brain you may have a stroke or something like that. It was scary, you know, and maybe I am putting it mildly when I say we panicked. And I was, like, yes but, like, it was in the superficial veins and not deep veins. 'Cause like if it's in your deep veins, that's when it causes trouble. But well, I mean I felt fine about it but I think being in the environment had an effect on me as some of the girls freaked out a lot … I mean, if I hadn't been a medical person then probably I wouldn't have been happy with it (HV19).

However, the participants with no medical background based their trust on their belief that the professionals were being truthful in the interests of professionalism. Most participants saw professionals as truthful and honest. However, this trust was often based on taking part in clinical trials that concluded without any side effects.

> [Talking about the risk of side effects] Yes, they said there were minor [side effects] and I trusted them to tell the truth because if not then they are outing their businesses on risk too. So they can't lie. I did not have side effects so that was okay. The volunteers were all fine. Usually this happens in other trials but the one was okay (HV2).

> I trust that they would be honest … and give me the support I need. I don't think they would lie, otherwise it will damage their image and reputation (HV15).

For these participants trust was based on the view that professionals will be obliged to tell the truth because misleading participants would not be in the interest of the business. In doing so, they

positioned professionals as primarily motivated by the need to protect their business interests. This is interesting because it shows how different conditions resulted in trust. Particularly for participants in the first part of this section, the shift from suspicion to trust seemed to emanate from becoming familiar with proceedings. However, participants with no medical training thought they had no choice but to trust the professionals.

> When you are on the trial, you only have one option but trust. They are your friends at that particular moment. So you have to trust them. Specifically because it's just medicines … So as long as the drug is fine, that it doesn't matter to me. It brings me some money and new medicines are made, then I am fine with it (HV2).

Furthermore, this shows how complex the notion of trust is in relation to risk when it involves lay public and professional interactions. Though participants might have been suspicious of professional explanations, in this research they eventually had to put their faith in the professionals (Walls et al. 2004). The conditions that brought about trust therefore were familiarity with research teams, organisational processes and routines, inside medical knowledge, and uneventful previous experiences on trials, while some felt that their dire financial situations meant that they had to trust professionals. This illustrates ways in which trust was born out of different conditions and impacted on people's perception of risk.

7.5 Risk and trust: negotiating and managing risks

Engaging with risk generally became routine (Lyng 2009) for healthy volunteers. Central to risk and stigma avoidance (Peretti-Watel and Moatti 2006) is the ability to negotiate and manage risk. Some participants in the study acknowledged that they avoided very risky trials. Accounts were common among healthy volunteers participants who had just started taking part in clinical trials; similarly those who had been involved in several clinical trials talked of feeling the same when they first started taking part in clinical trials – that FIHCTs were very risky trials.

> Yeah, I don't want to be a complete guinea pig. I must say I would rather a drug has been tested on others before, or if it's already on the market or the last stage and you are not taking the very high dosages. There are different phases, you see, like the phase I and the effects that come with it, so for me I wanted to avoid such trials because they are always associated with big complications. I would like to support science but only if it will happen in a safe way for me not being a complete guinea pig, no (HV14).

> I don't think I could do any drug ones [FIHCTs] just yet, not with me hearing too many bad things happening to people. I don't think I can do, like, a first-in-human trial. I would only do it if it's the very end of the stage in which they are trying it in people or they have done it several times on other people. I have seen drug ones [FIHCTs] before and when I have researched into them, they have kinds of side effects that I wouldn't want to take the risk (HV1).

Drugs that had not been tried first on humans were seen to be inherently risky, and mistrust of the system generally coloured the participants' view of clinical trials. As a result, some participants initially shunned FIHCTs.

> How do they expect side effects [in first-in-human trials] if they have not tested the drug on anyone? But I like the other phase trials … They already know that the drug works, but even if it was phase three there is a fair amount of caution that should be taken when you are doing clinical trials. You never know. While I think it is really vital … that drugs are tested thoroughly before they are made available to the wider public, I think there is a toss-up in selling your health and whether your health is ever worth any amount of financial compensation that you may get from taking part in the trial, because you can never be 100%, 100% sure (HV5).

> Initially I thought, "I can't do these because the risk is too high". This is because the way the human body responds to drugs is different to the, say, animals like

> rats [and] monkeys or whatever. You know, everybody has different enzymes and every species has different ways of dealing with drugs, so what may happen in a dog may be different to what may happen in humans, can't be replicated in humans (HV19).

> When I started I was like "I don't want to be a complete guinea pig", so is started with drug trials already in use, but with time I have found myself doing more very first phase drug trials … (HV33)

Participants had little trust in the institutions and systems involved in clinical trials. They tended to do their own research on active substances in the proposed investigational medicinal product (IMP) by browsing the Internet or consulting somebody they knew in the field.

> I went out of my way to find out about the company, found out about the drug, like really find out as much as I could before I did it … The first trial was also good because I had a friend who looked into the company and drug for me. And he assured me that it was sound. He himself is a scientist and he said they were an independent pharmaceutical company and they were being financed by some government (HV5).

> My second trial was with [name omitted]. That ticked my nerves because it was less organised in the sense that they did not have a schedule right away. Nurses where coming late and the instructions were not clear. Having those experiences therefore makes you less willing to go to certain places (HV4).

Some participants said they researched a drug to reassure themselves that the risks specified by the CROs matched what other sources said about the effects on human subjects. This illustrated the extent of mistrust that some volunteers had of corporations, though CROs provided information about clinical trials, healthy volunteers did not entirely trust them.

> I had already done all the research so I knew there wasn't anything really to worry about in terms of anything going wrong. I think it was just going into a hospital knowing that I knew some of what they were doing … I could have trusted them and just took their word for it like that. I was not sure, like, obviously they were taking blood and I don't have very good veins, so my blood is, erm, I am rubbish, so I wasn't sure how much that equated to whether I was going to go on to complete it anyway so, erm, yeah (HV5)

The issue of trust was a consideration throughout their involvement in clinical trials. Participants felt the need to trust (Walls et al. 2004) the professionals while they contended with the idea that professionals might not be entirely truthful about the risks.

> For me the most concern was that … even if I trusted the guys [professionals administering the trial], how can I know this is the drug they describe on paper and the effects they say it has? What if they write one thing on paper and give me another drug? … In the end, I had to convince myself that it is not possible, but even then, I struggle with that question every time I go into a clinical trial. I needed to be sure. I believe, though, that is it is possible, but in the end I just gave myself (HV9).

> I have some trust in these people, in the institutions doing their studies. When you are on the trial, you only have one option but trust they are your friends at that particular moment. So you have to trust them (HV2).

The vacillation between trust and distrust among the volunteers is in keeping with Keynes's view that individuals are not completely rational in their decision making (Keynes 2006). It is also in keeping with the argument of Alaszewski and Coxon (2009) that individuals use strategies that draw on existing relationships – intuitions that involve trust in maintaining relationships and distrust in circumventing individuals and events deemed threatening.

7.6 Safety in clinical trials

Trust and risk are central to safety, which is key to determining whether a clinical trial takes place. Safety in FIHCTs has been a priority since the 2006 Northwick Park incident (Schneider, Kalinke, and Löwer 2006) mentioned in the first chapter. Among the measures introduced after the incident was a process of dose escalation during trials: drugs would be administered in small quantities and gradually increased over time. Also instituted was a system of dosing participants in staggered intervals (Stebbings, Poole and Thorpe 2009). The regulations stipulate that a clinical trial will commence only if it has been certified safe by an ethics committee and the licensing authority. These institutions must conclude that "the anticipated therapeutic and public health benefits justify the risks and may be continued only if compliance with this requirement is permanently monitored" (Medicines for Human Use [Clinical Trials] Regulations 2004). The regulation makes provision for protecting subjects from physical and mental abuse and their rights to privacy in accordance with the Data Protection Act 1998. However, recent failures in clinical trials indicate how easily things can go wrong and the consequences this may hold for the subjects and for businesses. The next section examines professional and lay (healthy volunteer) views of safety and unexpected side effects in clinical trials.

Professional views about unexpected adverse effects in clinical trials

Among professionals, safety was perceived in two ways. This study identified those who looked upon safety as a functional issue independent of ethics, and those who looked at it as an element of the ethics process. For the former, safety was what they did, and some tended to follow procedures more flexibly than others.

> We don't deal with questions of money and volunteering. These are the remit of ethics committees. We are focused on the safety of the drugs, you know. Questions to do with drug dosages proposed safe for

> humans and things like that are our focus (Regulatory official 4).

> The ethics committees deal with issues of compensations. We have nothing to do with that. Our focus is safety, making sure units operate in keeping with guidelines, you know, and the drugs are safe for human use (Regulatory Official 6).

The view was common among regulatory officials that safety, like risk, could be identified and dealt with objectively. For members of research ethics committees, safety was of topical relevance, multifaceted and closely bound up with ethics.

> I think safety is part of what we look at. We have on our committees different professionals to make sure we understand these issues well. You know, safety is quite broad for us. [It] includes recruitment processes, information, target participants and, of course, the issue of compensation. So … yeah, it's quite broad I think (REC Official 10).

Current or past members of ethics committees saw the entire ethics process as being about safety and much more complicated than just the active ingredients in drugs. It encompassed recruiting, the venue of the study, provision of information and especially the participant's understanding of safety in the trial.

> What you want people to know when they taking part in a first-in-human study is that they are aware of the fact that basically you could die doing this kind of studies. And it starts there, I think. Unless people really understand that taking a drug that has never been tested on humans before … The risks may theoretically be very small but time and again we have incidents where things have not worked out the way we thought (REC Official 11).

> For me safety is paramount and its starts with how people will be treated, including what they will be tried on, and ends with aftercare support in place (REC Official 9).

Professionals generally expressed pride in the safety record of clinical trials. They felt that apart from the major incident in 2006 mentioned above, there have not been any fatalities in the last three decades. They felt there was no need for the existing regulatory system to be changed:

> I have been doing these studies for at least 30 years, erm, erm. There is always – although the overall safety record is good – there are, of course, adverse events, erm, and the adverse events might not be due to the drug and other adverse events being things that you think are due to the drug. Yes, over the years [we have had] plenty, erm, of it [adverse events] but the safety records [are] overall good. But yes, you do get adverse events… You might be surprised that the most troublesome adverse effects come from not new drugs but ones that are already existing, that we use for comparison (Professional 6).

> …what I am trying to say is that HV studies have been going on for a long time without major problems. And one of the reasons that they are relatively problem-free is because the first doses … are normally low. So the whole purpose of … doing the first-in-man studies is to determine the safety and also to see the pharmaco-kinetics of the drug. And so the dose is usually a very low dose and that is, erm, agreed by the pre-clinical assessors because it is based on guidelines from the FDA and recognised guidelines within Europe (Regulatory official 4).

Professionals generally saw the drugs tested in FIHCTs as being as safe as drugs on the market. They noted that fatalities in clinical trials were very rare.

Healthy volunteer views of safety and experiences of side effects

Contrary to professionals' claims that safety in clinic trials was better today than in previous years, volunteers spoke of the fact that for them adverse events were common in FIHCTs.

> I have had some experiences like three or four times, where some of us were told to go back home because someone [volunteers] was experienced or had some unexpected side effects. Some of those were quite serious but obviously we were not told the extent or how serious. So kind of lucky it wasn't me really but yeah it's common (HV24).

> What we experienced was unexpected and out of this world. It was akin to being on LSD [or] marijuana. It was noticeable in such things as hallucinations and loss of track of time, lying in bed for five hours. And you are not aware of it, giggling and laughing … but yeah, it was crazy and scary and worried … because it wasn't included in the list. And this is what happens, and I just got worried what more you expect (HV25).

> I have had quite a few such events but the most recent one was puzzling. But having said that it was a nerve-racking experience. It is not, like, an enjoyable experience. A huge part of me at that time wanted to get out coz it was scary. And the worst thing was that we were not told about these effects. They were unexpected. The people who took the drug with me that day were all, like, "Did you feel that or this?" Others were hyper or just much more giggly, completely out of character (HV 29).

The above accounts are interesting as they show how common experiences of unexpected side effects are in FIHCTs. In addition to accounts of experiences of unexpected side effects, participants in this research talked of how CROs might circumvent regulatory guidelines by avoiding the need to stop the trial. Some volunteers believed that clinical trial units managed events of unexpected side effects so as not to attract

attention and impede the progress of the trials. As mentioned in Section 6.2, a participant who experienced unexpected side effects was told she had psychosis.

> They try as hard as they can to stop trials going bad, you know. It may hurt their business or profits. Whether they have concern for people or protect people, I think it's more about protecting their image, interests and profits. And the cynical part of me would be to avoid such trials in the future but maybe do some reading around the trial. But not to put my faith in them completely (HV25).

> I was admitted in two trials a couple years ago that were cancelled because of the unexpected side effects. I was lucky. I was not the first person. We were sent home and never got called back for the trial (HV5).

The above accounts shows how volunteers could be made to feel that there was something wrong with them, rather than acknowledge the effects of the drug. Slanted information given by the professionals (Hillman 1993) in the trial meant that questions of risk did not become of topical relevance to volunteers and hence they continued with the trial (Schutz and Luckmann 1974). The lack of information about trials that have been cancelled due to unexpected side effects was mentioned in Chapter 3. Cancellations of trials are said to be common, although there is either no record of such trials or such information is not publicly accessible.

Volunteers' accounts of unexpected side effects were alarming. Some felt that their complaints about such experiences would go unheeded and hinder their prospects for enrolment in new trials. Many expressed concern about the long-term impacts of taking part in clinical trials. Professionals responded to such views by noting that the body gets rid of drugs in a short time. Men and women alike raised the issue of reproductive health, although the women expressed greater concern.

> I think [giggles] … I am still young, and I haven't had any kids or anything yet. So I don't want go into something that will jeopardise my future life. I am sure we all know that. We have seen on the telly people who have ended up with all sorts of, erm, side effects, so I don't want to, erm … end up like that (HV1).

> My only worry was on whether the drug did not have lifelong effects on the body. I want to have family in future and so I was not sure these drugs would affect this in the future. So I wouldn't have done a trial of that nature (HV3).

Some women volunteers avoided FIHCTs, regarding them as unpredictable and dangerous, while men regarded the possible effects on reproductive as being not of immediate topical relevance.

> I am aware that doing trials may affect your sperm count and all such things, you know, but I would follow what the trials do. I don't normally worry about this, to be honest. I do not find myself reflecting on the possibilities of a trial going wrong or not having children. Not my worry at the moment… (HV18).

This is interesting as it shows how participants were aware of the long-term implications of their involvement in clinical trials in terms. However, it is also important to note the differences in the relevance of the issue of reproductive health between female and male healthy volunteers. For some women volunteers, having a family was not a prospect.

> It has never crossed my mind [having children] because I don't want to have children and I don't think I will, so really it's not a problem for me (HV23).

7.7 Summary

This chapter has considered the connections between risk, safety and trust in FIHCTs. It was found that professionals hold strongly to the

idea that volunteers are rational and capable actors who are able to make informed decisions when provided with adequate information; it is the fault of the individual if he or she fails to understand the risks or fails to cope with side effects. Healthy volunteers contend with the widely held attitude that taking part in clinic trials is a reckless activity, akin to prostitution, and undertaken by morally unsound individuals. Some concealed their involvement from their families. Others took steps to avoid being seen as desperate volunteers and shunned FIHCTs which they considered very risky. Despite the stigma associated with being a healthy volunteer, for some participants in this study engaging with risk had become a habitual or familiar activity.

The chapter also examined how trust impacted risk perception, showing how previous experiences, familiarity with staff and procedures, and prior experience of medical settings were crucial factors in shaping individuals' trust in the professionals conducting the clinical trials. Also discussed was how unexpected side effects prompted some volunteers to question their safety and to reconsider their involvement in subsequent trials. CROs were shown to use the fragmented nature of the regulatory system to their advantage, downplaying unexpected side effects and slanting the information their staff gave to volunteers in adverse events in order to avoid the cancellation of trials. Professionals were generally found to view safety as functional issue. For REC officials on the other hand, safety was strongly linked to ethics, encompassing, among others, recruitment, provision of adequate information and aftercare support for participants in clinical trials. Many volunteers were less concerned about safety of the drug being tested than about the financial reward on offer. Most of them had decided to take part in clinical trials well before the consent process. The ethical focus on providing information at this moment to inform a rational decision rather missed the point.

Using Schutz's system of relevances brings about a nuanced understanding of the complexity of trust and risk taking behaviours. For instance in dealing with unexpected side effects by sending participants home is of topical relevance to CRO as institutions, as it means they can

keep the trial going and hence make profit. Therefore, giving slanted information becomes of motivational relevance. For the healthy volunteers, particularly for those with no medical training background, uncertainty of the clinical trials was of topical relevance and to deal with uncertainty in these contexts trust in professionals became of motivational relevance. Using Schutz's system of relevances in this way therefore aids the analysis of both professional and lay conceptions of risk and safety, and also of institutional and individual actions. For instance, structural definitions of "normal work" influence healthy volunteers' perception of their involvement in clinical trials including how they feel about themselves. In addition, participants' accounts of trusting professionals or relying on previous experiences, which in Schutz's terminology would be their stock of knowledge, relates to what Bloor (1995) refers to as a "monothetic" process of decision making in cases where individuals are familiar with the stimuli or when actions become habitual as outlined in Chapter 2.

Chapter 8 Conclusion

8.1 Introduction

In this final chapter, I review the previous seven chapters to address the aims of this thesis. In the research, I have attempted to locate my analysis of policy documents and interviews with the actors in first-in-human clinical trials in the institutional and social context that shapes their participation. This approach has been useful in developing a nuanced understanding of policy context and the experiences of healthy volunteers in FIHCTs. Contextualising the topic has enabled me to study healthy volunteers as subjects with the ability to resist and negotiate complex and often conflicting socio-economic and political milieus in clinical trials. In reviewing the steps I have taken in this thesis, I draw out the implications of the research as a whole. These centre on the adequacy of existing regulatory structures in protecting healthy volunteers and how risk in clinical trials is perceived by the actors.

8.2 Policy and Regulatory Terrain

I introduced the thesis with a description of the background leading to the development of healthy volunteering in clinical trials. It considered the commercial and regulatory context in which clinical trials take place, the growth of the pharmaceutical industry, public demands for cheaper, better and safer medicines and the government's provisions to balance support for industry with adequate regulation and ethical oversight. Regulation of human involvement in clinical trials is discussed in Chapter 2. It is shown to be influenced by the bioethical conception of human subjects as being capable of representing their own interests. An increase in clinical trials and the growth of the pharmaceutical industry have made healthy volunteers a valuable resource for pharmaceutical corporations. In neoliberal terms, the state facilitates such growth under the banners of individual liberty and the free-market economy while volunteers are exposed to exploitation in an unequal engagement with powerful organisations and institutions.

The need for a policy and regulatory framework that deals with such challenges effectively and transparently is clear. However, business and healthcare priorities have undue influence on human involvement in clinical research and the role and experience of healthy volunteers. Legal and policy frameworks promote autonomy of individuals and markets to protect the safety of human volunteers in clinical trials, improve healthcare for the public, and foster business growth. However, pharmaceutical corporations do not necessarily share these commitments to the wider public good (Goldacre 2013; Rajan 2006).

Policy discourse tends to present healthy volunteers as being positioned outside commercial transactions; it overemphasises altruism and voluntarism as motivations, as shown in the Nuffield Report (2011), despite the highly commercialised context of clinical trials. Anthropologists Petryna (2005), (Rajan 2006) and Cooper and Walby (2014) allude to the commercial and political contexts in which value is created in medical research and the practical challenges they bring, highlighting that healthy volunteers need more protection than the industry offers. Discussions about regulation and safety centre on the notion of informed consent and the need to protect patients, children and those considered mentally incapable of making rational decisions. There is also a tendency to conflate volunteers with patients, whether they are involved in routine healthcare or clinical trials, and to see the provision of adequate information as the solution to any ethical dilemmas that might arise in clinical trials. However, there is little understanding that the vulnerability of participants might well extend beyond matters of physical and mental health to include the socio-economic and socio-political contexts in which they live. I draw on the conceptions of vulnerability of Turner (2010) and Fineman (2008) and look beyond the medicalised policy definition of vulnerability associated with victimhood or pathology. I argue the need for a broader view of vulnerability that challenges the idea of a capable, independent and liberal subject.

Specifically in reference to healthy volunteers, consideration should be given to their financial difficulties, the social attitudes they contend with

and the routine interactions with professionals that influence their encounters with risk. This raises two important questions. First, if the regulatory framework ensures that individuals take responsibility for their decisions, will it be clear when things go wrong in clinical trials that they were deemed capable of giving rational consent? Second, what should be made of the uncertainties surrounding healthy volunteers' consent for the use of their bodies in clinical trials?

The problems raised by the volunteering in clinical trials of individuals who are financially needy or desperate and who may not fully understand the risks are not resolved in existing policy and regulatory frameworks. Regulation should take account of diverse social circumstances and of the interactions in which consent is given. On another level, the challenge is to ensure a viable commercial milieu which establishes FIHCTs as legitimate while facilitating the flourishing of science and industry to meet public expectations of better healthcare. The problem is that there is a tendency to position healthy volunteer involvement as existing outside of and separate from the commercial domain. While the potential for exploitation is acknowledged, monetary reward for participation is seen as compensation for volunteers' inconvenience, discomfort and time in the trials. I argue for a discourse of policy on human involvement in clinical trials that addresses not only compliance with regulations, but also the need for a deeper understanding of how and why individuals decide to take part in clinical trials in the first place, and whether they bear too much responsibility for the risks they take. The policy and regulatory framework should consider the wider social context and the complex nature of the exchanges to guide human involvement in clinical trials.

Regulatory and policy terrain – "fragmented" regulatory system

As discussed in Chapter 4, the uncertainty associated with results and outcomes of trials elevates the importance of technical and practical aspects, and less attention is paid to the context in which the trials take place. This study exposes the fragmented nature of the regulatory terrain.

One reason for this could be that the process of regulating first-in-human clinical trials is relatively new. Before 2004, the application process only required ethics approval and peer review of the trial proposal (Castle and Marshall 2007). It is not clear how this was done in practice, what information was given to the ethics committee and whether there was a system to police applications.

Important changes have happened in the past 10 years and especially since the Northwick Park incident of 2006. The application process requires safety checks by the MHRA in cooperation with ethics committees. Dose escalation procedures are in place. Phase accreditation schemes have been introduced in which clinical trial units apply to be recognised as early phase trial units. Principal investigators in early phase trials are required to hold a diploma in human pharmacology. In response to concerns about fragmentation in regulation, the Nuffield Report 2011 endorsed a proposal to bring about the establishment of a health research authority (HRA) to monitor practice, regulation and governance of health research involving patients. The institution has been set up, but as an authority and not as the agency responsible for organising and co-ordinating the national research ethics advisory panels and the National Research Ethics Service. It remains unclear how the HRA is meant to fill in the gaps in the fragmented regulatory process. This is because at the core of the HRA is the NRES, which has always been in place, focusing primarily on organising and supervising local research ethics committees (LRECs). It remains to be seen whether its introduction has made any difference to the regulatory process.

A key focus of the research was professionals' views of regulation – pharmaceutical company researchers and managers, regulators and ethics committee members. In the interviews, it became clear that their views about the adequacy of measures to protect participants in FIHCTs were shaped by the institutions they worked for or were affiliated with. Professionals agreed that regulation today is better than before but that there is room for improvement. Members of ethics committees in particular expressed concern about regulating payments to healthy

volunteers, citing a lack of clear guidance. Their concerns were confirmed in the analysis of policy documents and guidelines. Some regulators saw the issue of payments as matter for ethics committees; members of ethics committee acknowledged their lack of influence in the matter. This illustrated how the regulatory framework for FIHCTs relegated issues of concern to healthy volunteers to the "no man's land" of clinical trial regulation. Professionals working for contract research organisations regarded the regulatory regime as adequate. However, issues of topical relevance, as might be expected, concerned the impact of over-regulation on business. They feared that any more changes to the existing regulatory framework could drive business away from the UK.

8.3 Accounts of motivations for involvement in clinical trials

The study showed monetary rewards to be the primary motivation for volunteers. They generally did not want to be involved in clinical trials; rather, their decisions to take part were influenced by their social circumstances such as excessive debt, unemployment and inadequate incomes. For most, taking part in clinical trials was initially seen as a last resort or a one-off commitment to address an immediate financial need. Many became repeat volunteers, usually after incident-free trials and interactions with supportive staff. Participants also tended to feel that they owed researchers something in return for helping them when they were having financial problems the first time they volunteered. As a result, they expressed willingness to come back and volunteer even if, in some cases, it was free of payment or for reduced pay.

A minority of volunteers cited altruism as a motivation. Others, motivated by monetary rewards, tended to justify their participation in ways that implied social acceptability. The term "volunteers" was found to be qualified by the complex social and financial circumstances and power relations in which the individuals found themselves.

8.4 Healthy volunteering as "passive labour"

On the other hand, the unseen, and often unconsidered by the public, neoliberal forces that shape volunteer recruitment and interactions between the public and commercial medico-technological innovations contribute to how the public view their bodies in their engagement with risk. Bodies have become tools that are used to make a living by taking part in clinical trials for alluring rewards on offer from the research companies. Important contributions have been made to this discussion by anthropologists Fisher (2007), Elliott (2008) and Abadie (2010); their works have explored how socio-economic and socio-political forces influence healthy volunteer involvement in clinical trials. However, official government regulatory – specifically bioethical – and industry discourse has situated healthy volunteering as being mainly altruistic and voluntary. Human involvement in commercial clinical trials involves an economic exchange of the body. The healthy volunteers I interviewed were highly aware of the nature of the exchanges they were involved in and explicit about how they felt about the process. Those who talked of healthy volunteering as an exchange compared it to prostitution – a straight exchange of the body for money.

Arguably, healthy volunteering has parallels with emerging research interests in surrogate mothers (Waldby and Cooper 2008; Cooper and Waldby 2014). The exchange in clinical trials is what I call "passive labour". Accounts of such "passive labour" have parallels with Waldby's (2004) concept of "biovalue", in which biological products attain value in medical research. The healthy volunteer participants in this research saw a need to work on their bodies to maintain their value, even if they did not use the term "biovalue" to describe it.

8.5 Rational consent, trust and risk

The literature review began by considering how sociologists have studied rationality, drawing on the work of Wynne (1996), Horlick-Jones (2005), and Kemshall (1998), among others. While such studies have attempted to understand how people make decisions and view risk in uncertain situations, bioethical conceptions have been influenced by

conceptions of individuals as rational actors. Sociological discussions have drawn attention to the ways in which individuals are not always seen to make rational decisions for they are embedded in a social setting. Instead, their decisions, which might as well be rational, are often contingent on the context and situations in which they find themselves. Within bioethics, which is shaped by liberal assumptions of individualism, the principles of autonomy, capability and rational consent are seen as a necessary process and part of human involvement in clinical trials (Wolpe 1998). Despite many sociological and bioethical debates questioning the suitability of such assumptions of rational consent, consent based on the provision of information is central to the policies guiding human involvement in clinical trials. The consequences of the dominance of bioethics are illustrated in the discussion about the social context in which individuals make decisions to engage with risk. Factors to consider include relationships of power and trust and the socio-economic context, often featuring debt, unemployment and even homelessness. As discussed in Chapter 2, the bioethics model negates how these factors shape risk perceptions and decision making. Clearly, within the bioethical understanding of rational consent, there is little consideration of the underlying social processes and of how they influence reasoning (Kleinman 1999).

I used sociological and anthropological research into human involvement in clinical trials to illustrate how these contexts shape decision making. Substantive research in this area has tended to focus on the issues arising out of the role of patients as research subjects in clinical trials – their responses, experiences and views, and questions of diagnosis and treatment. I showed how human involvement in FIHCTs is closely linked to new forms of citizenship and shaped by social and moral expectations of citizenship, which in turn influence public views and experiences of medical research. Rose and Novas's (2004) concept of biological citizenship was shown to have resonance for human involvement in clinical trials. Current developments, such as the UK government's growing support for the pharmaceutical industry in the development of science and improved healthcare delivery (Will 2011) and the creation of

the Biobank (Tutton 2009; Mitchell and Waldby 2010) are examples of ways in which citizenship is being reconstituted to focus not only on civic rights but also on the biological aspects of citizenship. In this context, the focus is on the duty of citizens to contribute to the development of science for the betterment of societal health. The discourse of healthy volunteering as a gift relationship has thus flourished. However, assumptions of how biological citizenship and gift relationships work in practice preclude wider discussion about individual moral reasoning and the milieu in which gift relationships and biological citizenship take place.

8.6 Accounts of safety and risk strategies

This study has shown how healthy volunteering tends to be viewed socially through a moral lens, with the result that those that who take part in clinical trials are likely to be stigmatised (Goffman 1963; Peretti-Watel and Moatti 2006). The participants in this research took steps to avoid such stigma by concealing their involvement in clinical trials. They also had to contend with the risk of adverse events, including unexpected side effects, from drugs being tested on them. Chapter 7 shows that for some participants in clinical trials, the topical relevance of risks is often shaped by the social circumstances in which decisions about risks are made (Peretti-Watel et al. 2007; Lyng 2009). For instance, when faced with mounting debts, they focus less on the risks in clinical trials than on the financial problem they are trying to solve. They may therefore not fully absorb information about risks. Their perceptions of risk were further influenced by the trust (Walls et al. 2006) they developed with professionals and institutions administering the trials and by their previous experiences of trials, especially in the absence of adverse effects.

Some regulators – notably those involved in assessing trial applications and inspecting clinical trial units – saw safety purely as a matter of the composition of the drugs to be tested; safety for them was a functional matter that could dealt with objectively (Fiorino 1990). Seeing safety as independent of ethics in this way is problematic because the narrow technical focus excludes the important influence of power

relations, enticement and relative disadvantage in clinical trials. Other regulatory officials, ethics committee members in particular, saw safety as multifaceted and as encompassing recruitment, rewards and the degree to which participants are informed about the risks. The debate also highlights a lack of wider communication among professionals about the payment of rewards and its impact on the informed consent process.

Regulatory and corporate professionals generally viewed healthy volunteers as capable and rational actors, raising questions about the relationship between privilege and agency and the neoliberal framings of contemporary notions of choice. Such a view of healthy volunteers is of motivational relevance to regulators and industry because healthy volunteers are regarded as being responsible for their involvement in trials, reducing the extent to which institutions will be held accountable for any adverse consequences.

8.7 Re-reading Schutz: system of relevances and human involvement in FIHCTs

Turning to Schutz's (1970) system of relevances as a conceptual tool for explaining human involvement in clinical trials, introduced in Chapter 2, I critiqued bioethics and rational choice theory for emphasising rationality and capability in the decision-making process, noting that it is contingent upon issues of trust and power which individuals have to negotiate. The idea of rationality fails to take into account behaviours that may be habitual and thus undertaken without much prior thought. Besides, it overemphasises ability and choice. To understand healthy volunteering better, therefore, requires a framework that offers a wider view of human involvement in clinical trials, one that considers restrictions and resistance alongside rational and irrational, active and passive aspects.

It is against this background that I adopted Schutz's phenomenology of system of relevances in explaining human involvement in clinical trials. The theory focuses on actions or behaviours that are often overlooked and in doing so explores taken-for-granted behaviours – what Schutz refers to as the "world of routine activities" (Schutz 1970:139).

Although Schutz has been criticised for his reference to a philosophy of consciousness, for being overly subjective and for ignoring individual interactions with structures, power and how these constrain human behaviour (Goettlich 2011), the concepts he introduces can add to our understanding of this broader terrain of decision making. These theoretical tools help to analyse institutions, power, individual decision making and a range of social contexts.

The significance of exploring human involvement in clinical trials becomes clear when we consider what Schutz calls "intrinsic" and "imposed" relevance. By this he means the ways in which relevances can be experienced as internal or imposed by external factors, such as laws or prevailing attitudes in society, or as voluntary or involuntary. Imposed relevances can also refer to the institutional context in which agency takes place – the rules, customs and values and the wider political milieu, including the capitalist economy – and how they shape how we experience and feel about ourselves and the choices we make.

Turning to the data on healthy volunteering, it was suggested in this thesis that the system of relevance provides a tool for explaining healthy volunteers' decision making. Few of them had considered taking part in clinical trials; instead, they had done what they could to make a living in more conventional ways such as getting a job. However, when confronted with mounting bills and excessive debt that could not be dealt with by using conventional means such as finding a normal job or borrowing money, and when presented with an opportunity to take part in clinical trials, healthy volunteering became of topical relevance – they had to think of the benefits of this option (in other ways a case of interpretative relevance) and its solving of their financial problems. This interpretation had to be in keeping with their existing stock of knowledge and yet was also shaped by wider institutional influences, such as the stigma attached to volunteering, the rhetoric of informed consent, trust in institutions, and the idea of the gift relationship and biological citizenship. In sum, these factors could be understood as motivational relevances.

While this applies to healthy volunteers' motivations for taking part in clinical trials, the same can be said of their engagement with risk. Some volunteers saw engagement with risk as normal, simply an occupational matter. In this sense, their perception was well within the taken-for-granted realm of Schutz's scheme of relevances, particularly when healthy volunteering became habitual and healthy volunteers became accustomed to the risks. As long as they were confronted with the same stimuli and same processes with the same outcomes, they did not consider the risks to be a problem. In fact, the more often they took part in clinical trials the less inclined they were to question the process. Additional factors, such as the trust they had in the professionals doing the research, provided the basis for the stock of knowledge they had regarding the safety of clinical trials. For most of these participants, the issue of risk did not require further investigation or explanation.

However, the meaning of risk changed when trial participants were faced with unexpected side effects. Then they would question the experts who were administering the trial and look for explanations as to what may have gone wrong – an example of interpretive relevance. Some volunteers assumed there were rational explanations for why certain things were done a certain way. Others who experienced adverse events or had misgivings occasioned by a lack of satisfactory explanations by staff members shunned certain kinds of clinical trials or avoided further involvement altogether – an example of motivational relevance.

As discussed in Chapter 2, the decision-making process does not always flow in an orderly manner; rather, it is a fluid process. Some decisions are not just about addressing problems that can be explained but also about resisting conventional means of seeing the world. Some volunteers disagreed that their participation in clinical trials was reckless; they questioned common attitudes about work and saw their involvement as resembling paid labour, which often comes with risks. While a minority gave personal values and beliefs as their motivation, most cited the desire to resolve personal financial problems.

The "imposed" nature of these relevances related to ways in which healthy volunteers' involvement was defined and regulated by institutions, which in turn enabled and yet constrained agency. Schutz's theory is also useful in analysing institutional policies in showing that power and influence do not rely only on the presence or absence of capability and rationality, but also on the degree to which behaviours and actions are shaped by the "imposed" nature of the topical, interpretive and motivational relevances of everyday life. For instance, the labelling and stigma associated with healthy volunteering as an activity undertaken by people who are reckless arises from the differences in the relevances between those who do and do not take part in clinical trials. For some, initially taking part in clinical trials may not be of high relevance. However, in a society where what you do for a living is a marker of your success in life and reflects your social class and education, taking part in clinical trials as a volunteer becomes highly relevant. The supposedly objective interpretation by those who do not take part in clinical trials influences one's view of her/himself and defines them as being part of the "in-group" – in this case healthy volunteers. Schutz's theory offers a tool to analyse the perspectives of the individual who is subjected to prejudice and the institutional context in which healthy volunteering occurs.

The differences in healthy volunteers' attitudes about risk and strategies for dealing with it, as highlighted in this research, can certainly be understood through Schutz's system of relevances. The healthy volunteers who talked of engaging in clinical trials without concern for the risks involved could not be distinguished from those who were careful about risks because of their differences in risk perception but because of the context – specifically their experiences of adverse effects or financial situation at the time they decided to get involved in clinical trials. Although for many healthy volunteers in this research, risk avoidance was topically relevant, they found that their decisions and actions were constrained by the social and institutional context in which decisions had to be made. Those who avoided risks did so by using strategies which gave them

control over certain aspects of the process, though only to a limited extent (Bloor 1995).

Understood in this way, healthy volunteering is an engagement with complex power relations in a setting of competing and conflicting personal and commercial interests. It becomes clear that use of the term "volunteering" can be misleading and obscure the inequalities that give rise to the exploitation of human beings for the value that their bodies possess. Rather than seeing trial volunteers as reckless individuals, a more nuanced understanding of healthy volunteering would take account of the circumstances and context in which they decide to participate in clinical trials.

This thesis has used Schutz's theory of system of relevances to explore the ways in which individuals are able to reconstitute themselves in responding to their varying financial situations. It was shown that participants in this research, particularly healthy volunteers, recognised their participation in clinical trials as a commercial transaction, and they came to view their bodies and themselves differently. How they rationalised the exchange and devised ways of negotiating this complex relationship made it clear that they do not take part in clinical trials indiscriminately. On the contrary, their decisions were found to be contingent on several factors that challenge the normalised conceptions of healthy volunteers revealed in Chapter 5, which portrayed them as careless and motivated by a desire to make quick money. In fact, the volunteers interviewed in this study were found to be mostly educated and held well-paid jobs. In view of the discussions in Chapters 6 and 7, it appears that healthy volunteering in FIHCTs provides a space for individuals to experience what it means to have biovalue and to be consumers and participants in the Western neoliberal marketplace as they challenge, resist, negotiate and exploit the commodification of their bodies in the form of *passive labour*. In this thesis I have highlighted both positive and negative aspects by suggesting that human involvement in clinical trials is not done out of an entirely free, unconstrained "choice" but that it is an outcome of the interaction of personal circumstances with wider socio-political

contexts which makes individuals get involved as they reflect on their social situations, practices and relationships within neoliberal capitalist economies.

In summary, using Schutz's understanding of relevances and their role in social interactions allows for a sympathetic concept of healthy volunteers, rather than the common but incomplete portrayal of volunteers as capable, rational subjects or as reckless and greedy. It highlighted ways in which involvement in clinical trials gives healthy volunteers space to construct identities informed by a sense of their biovalue. At the same time, Schutz's ideas allow us to take into account how social-institutional relationships influence volunteer involvement in clinical trials. Far from seeing Schutz's system of relevances as being entirely subjective, considering the imposed and involuntary aspects of his theory therefore requires taking into account the ways in which the vocabulary of bioethics and corporate interests give rise to the creation of biovalue and sets the terms on which healthy volunteers and corporations interact in clinical trials. However, there are aspects of human involvement in clinical trials that this theory cannot explain, an issue I address in the last section as I discuss the policy implications of my research.

8.8 What could be done to improve protection of healthy volunteers in medical research

There is a need to acknowledge that healthy volunteering is a form of work, which I have called "passive labour", and thus to ensure the provision of safe and fair working conditions. This should go beyond the system in which consent is given, to clarify the processes for dealing with CROs to prevent bullying or coercion, problems that were described by some participants in this research. A framework in which impartial information and advice are made available to volunteers would be useful. Support services for volunteers in clinical trials are provided by the same companies that administer the trials, and it is possible that many healthy volunteers have faced situations they would rather have avoided if they had had adequate representation and impartial advice. Ultimately, healthy volunteers should have a bigger say in important decisions about the ways

in which first-in-human clinical trials are conducted and regulated. They have no platform to campaign for better conditions or improved rewards. By contrast, patients are represented by patient organisations and charities who ensure they get a better deal in clinical trials.

The study has shown a need for robust discussion among professionals, regulators and healthy volunteers on how rewards are calculated, to ensure that they are fair and represent good value for the volunteers, rather than leaving it to the industry to determine what to pay them.

Healthy volunteers should have a means to provide feedback about their experiences in clinical trial units – a web-based platform is one possibility. This could also be a forum to rate facilities and report problems about contracts, for instance, or payments when dropping out of a trial. Follow-up mechanisms after trials could be improved by providing clear guidelines about timeframes and for record keeping. The MHRA and ethics committees could be responsible for policing this.

A major concern of mine at the beginning of this project in 2008 was the lack of industry consensus on the use of volunteer registers to avoid over-volunteering. Since then the registers have been transferred to the HRA and NRES but the impact this will have in preventing over-volunteering remains to be seen. Providing an EU-wide register would benefit the industry greatly by helping to ensure that volunteers are not over-exposed to certain chemical agents when taking part in clinical trials across international boundaries. There is also a need to investigate drug interactions in healthy subjects who take part in multiple studies and the appropriate intervals between studies. At the moment, although three months seems to be a standard time limit, there is no consensus among experts about drug interactions within this time frame. Such clarity would help to direct support and information in the right direction – including to human volunteers themselves.

Clearly, the measures proposed here would provide better protection for human subjects in clinical trials. But would the

pharmaceutical industry support provisions that might affect its business in a system that it regards as adequate? Also, the proposal to give volunteers a greater say in decisions about reward and conditions in clinical trials might be difficult to implement because they are not found in one place; bringing them together, even online, would require a great deal of organisation and mobilisation, although databases now controlled by the HRA and NRES would facilitate such an initiative. Besides, implementing such changes would require substantial funding.

Implications for further research

This was a qualitative study, juxtaposing perceptions and experiences of risks in clinical trials by healthy volunteers, regulators and professionals in pharmaceutical corporations in the UK. The findings reflect the depth and breadth of issues that influence human involvement in FIHCTs. Some issues that are not explored in this research deserve closer attention. First, a longitudinal study that follows healthy volunteers over long periods and through various clinical trials would have added another dimension to this study, by examining more closely the behaviour and strategies of healthy volunteers to avoid detection when over-volunteering and of how they move between trials. However, a longitudinal study would have narrowed the participants and taken away the diversity of participants present in this current study. A strength in this study is that the participants were from a wide range of social situations and positions, something that is missing in existing research on this subject, for example in the US.

Another topic for further research would take gender as a topic, exploring the different ways in which men and women experience being in clinical trials. The discussion in Chapter 6 raised the topic only briefly due to limited space. A study of the gendered aspects of healthy volunteering would draw on interviews and data analysis and would require a different kind of recruitment strategy to ensure equal representation. Likewise, this study could have considered the issue of race and ethnicity in the practice of clinical trials, and the same practical considerations would apply. The

sensitive nature of the subject in my study meant that I could not focus on this subject.

A European comparison would also have added to my research by demonstrating how EU regulations are interpreted and implemented in different member states and by documenting the experiences of healthy volunteers in clinical trials across national boundaries and in different socio-political and economic contexts.

Despite these gaps, this study has answered the four questions introduced in Chapter 1. It has added to research on human involvement in clinical trials in the UK, which mainly focusses on patient groups, by providing the first empirical academic account of healthy volunteering in FIHCTs in the UK and thus opened the way for further research and theoretical work on the topic. The study has raised important questions about the practice of regulation and about social justice and the value of human bodies in medical research to individuals. It has exposed the ways in which neoliberal assumptions frame the conduct of clinical trials through bioethical and regulatory discourses and influence the relationship between choice, individual liberty and inequality in healthy volunteering. This final chapter has reflected on the conclusions we can draw about the ways in which the risks and rewards in research participation are understood and shape motivation for involvement in clinical trials, and about the implications for regulation.

In concluding six years of challenging but fulfilling work and about eighty thousand carefully selected words, it is only appropriate to return to what my intentions were in doing this research. My aim was to bring about debate that would lead to a reconsideration of how healthy volunteering in clinical trials is conceived by the different professionals involved, and even the public. I close with an extract of a comment from one of the participants in my study, a regulatory official who read sections of this work:

> Though you sometimes rather strongly criticised my field of work … [reading] this has made me start to think differently about healthy volunteers and why they take part in clinical trials. Maybe before I was naïve and did not consider how complex it is, and that payments and other factors have a greater impact on people in some financial situations than I had thought … I will not look at clinical trial advertisements or even trial applications on my desk the same (Regulatory Official 8).

I believe I can confidently say that this project provides a platform for developing a considered sociological understanding of human involvement in clinical trials which has at its root questions of inequality and justice, and about framings of risks, rewards and regulation in FIHCTs.

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Appendices

Appendix One: Interview Package

Interview schedule for ABPI

1. Talk me through how you got into this job?
2. What does your job involve?
3. Have you ever been involved in responding to cases of adverse reactions in first in human clinical trials?
4. How do you deal with cases of AR?
5. I know the Northwick Park incident park incident is an extreme case, but did this have any impact on how you worked with industry?
6. If so how?
7. What is your view about the role of monetary rewards offered to volunteers in first in human trials?
8. Does ABPI have any influence on how industry pays volunteers?
9. What is your view about the argument that payments are an undue inducement on volunteers and compromise the informed consent process?
10. Related to payments is the problem of over volunteering, what has ABPI done about this problem?
11. What is your view about volunteer registers?
12. Why in your view is there no consensus on volunteer registers in industry?
13. Has ABPI been involved in discussions on this issue with the industry?
14. In your opinion how is the current regulatory framework impacting industry? Are there too much regulations/ too little, etc.
15. What would you say to the argument that ABPI has far too much influence on the regulatory process and should instead leave some of its roles to MHRA?
16. What is ABPI's views about what happens to over volunteers after the study?
17. In the guidance that you give to industry on first in human trials, do you ever consult with volunteers on such matters?
18. If not why? If yes how?
19. Do you work with organizations that specifically advocates for healthy volunteer interests
20. If not why?/if yes which ones?
21. Are there issues I have not asked you think I should know about your job to better understand your role as ABPI?

Ethics committee

1. How did you get you involved in REC?
2. Following changes on how FIHCTs should regulated in 2004, how has your work changed?
3. Will you talk me through the assessment process?
4. Are there any differences in your experiences of reviewing commercial trials applications compared to your experiences of reviewing academic or investigator-initiated trials?
5. What is it like assessing reviewing FTIH clinical trials?
6. What is your view about risks involved in phase I clinical trials
7. What is your view about monetary rewards offered to volunteers?
8. How do you ensure that the rewards paid to volunteers are appropriate for each study?
9. In your opinion how adequate are measures to address this issue to ensure participants are not exploited?
10. What contributions do you make to help applicants with decisions on monetary rewards?
11. What does legislation say about rewards?
12. What would you say about monetary rewards compromising the consent process?
13. What would you say about the view that there is a potential strain on one hand to enforce regulations and the other the prospective therapeutic value that a drug may possess impacting on your practice as REC members?
14. I know the 2006 Northwick park event was rare event but how did that make you feel?
15. Have you ever been involved in investigating or dealing with trials that have gone wrong apart from Northwick Park incident
16. Following the Northwick park incident a lot of work has been done to improve practice, what would you say about measures to address the issue of rewards in FTIH trials after the incident?
17. In your work, have you worked or interacted with advocacy groups that represent HV interests? (or volunteers themselves?)
18. If not why do you think it is so? (if yes what are they?)
19. Recently the APBI issued a compensation guidelines to industry, where you involved in the drafting of the guidelines?
20. Do you know if volunteers were consulted in the formulation of these guidelines?
21. If not what do you think is the challenge in getting volunteers involved in such consultations?
22. How do LREC network with organizations such MHRA & ABPI?
23. How do you monitor the implementation of these guidelines in practice?

24. How does the LREC monitor the effectiveness and quality of the volunteer consent in practice?

25. Are there things I have not asked you think I should know to better understand the/your role of REC or as REC member?

Interview schedule for professionals in CRO's

Initial questions

1. Tell me how you got into this job? (Prompt What motivates them in doing this job?)

2. Tell me about your early years in this field?

Intermediate questions

3. What is it like working as part of a team involved in first in man studies?

4. Tell me your experience in dealing with uncertainty?

5. How do you go about preparing participants for the trials?

6. Have you ever had to deal with adverse reactions in first in man studies?

7. Tell me about your experience in dealing with adverse reactions in studies you have been involved in?

8. I know the Northwick Park incident park incident is an extreme case, but what were your observations with regards to volunteering in FTIH clinical trials after the incident in terms of numbers and interests?

9. What kinds of people volunteer for first in human studies?

10. Why do you think?

11. What is your view about the monetary reward offered to volunteers? How is the reward calculated?

12. What happens to volunteers after the study?

13. Do you know of organizations that represent or advocate for healthy volunteers interests?

14. How does your organization ensure that volunteer interests are considered in research?

15. What are the main regulatory issues that come up in your work?

16. Could you describe your experience in preparing for an inspection from GCP inspectors?

17. How has your work changed following the 2004 regulatory changes?

18. What impact have the changes had on the conduct of first in man studies?

19. How has your experience with GCP inspectors affected how you deal with/view volunteers?

20. How do you monitor/report the implementation of these guidelines?

21. In your opinion how clear are the guidelines from regulatory bodies with regards to monetary rewards to be offered to volunteers?

22. Do you usually have the same people volunteering? (prompt How do you deal with this?)

Ending Questions

23. Are there things that have occurred to you as we were talking that you had not thought of before?

24. Is there something I have not asked that you think I should know to better understand your work and experience in first in man studies?

25. Is there anything you wish to ask me?

Interview schedule for Staff at regulatory bodies-Inspectors

1. Tell me about how you got into this job? (follow up questions: What is your role? What motivates you in doing this job?)
2. Could you describe your views about licencing and regulation of first-in-man clinical trials before your organizations got involved in inspecting first-in-man trial units?
3. How have your views changed now that you are involved?
4. Tell me what it is like inspecting units were first-in-man studies are conducted?
5. How has your work changed since 2004 when your organization started to regulate first in man studies?
6. Talk about challenges inspectors face in dealing and inspecting first-in- man units?
7. Will you talk me through the inspection process?
8. What is your view about monetary rewards offered to volunteers?
9. Will you talk about the adequacy of current measures to regulate this issue to ensure participants are not exploited?
10. What contributions do you make to make to help applicants with decisions on monetary rewards?
11. What challenges does your organization face in dealing with this issue?
12. The 2006 Northwick Part incident involving the TGN 1412 was an extraordinary and extreme incident, what were your feelings when you heard about the incident?
13. What impact did the incident have on your roles as inspectors of clinical trial units?
14. How does the issue of risk and safety of volunteers fit into your role as an assessors?
15. What challenges do you encounter in dealing with issues of safety of volunteers in clinical trials?
16. Talk to me about how you balance the potential strains on one hand related to regulating practice to promote safety and on the other to make sure the industry flourishes?
17. How do you network with other agencies, such as LREC's ABPI etc, in the process of regulating first in man trials?
18. How do you ensure that wider EU policies are implemented on the ground?
19. How does (name of organization) monitor the implementation of these guidelines in practice?
20. How does (name organization) monitor the effectiveness and quality of information given to volunteers by CRO's in practice?

Interview schedule for volunteers

1. What is your occupation? Current or previous
2. What would you describe your ethnicity as?
3. What would you describe your social class to be?
4. How did you hear about the clinical trials?
5. How did you get involved?
6. What do you think about the recruitment process?
7. At what stage did you decide to take part in the trial?
8. Is this your first time as a volunteer or have you taken part in other trials before?
9. If so, how long have you been doing this?
10. What motivated you to take part in this/these trial/s?
11. How important is the monetary reward on offer to you?
12. Do you think you have all the information necessary to help you make a decision?
13. What is your view about the risks involved in trials?
14. Have you ever experienced any adverse effects from trial drugs in your time as a volunteer?
15. If so how did you deal with that
16. Do you think you have adequate information about possible effects and what support you would have in case of severe effects?
17. Do you know of any channels of communication/support available for you if you have a an issue with during or after the research?
18. How do you ensure your voice is heard on issues of clinical trials if you have any concerns?

University of Sussex

CONSENT FORM FOR PROJECT PARTICIPANTS

PROJECT TITLE: **Risk, Reward and Regulation: Exploring Regulatory and Ethical Dimensions of Human Research Participation In Phase I Clinical Trials In The United Kingdom**

Project Approval Reference: 1112/12/08

I agree to take part in the above University of Sussex research project. I have had the

project explained to me and I have read and understood the Information Sheet, which I may keep for records. I understand that agreeing to take part means that I am willing to

- Be interviewed by the researcher
- Allow the interview to be audio taped
- Make myself available for a further interview should that be required

I understand that any information I provide is confidential, and that no information that I disclose will lead to the identification of any individual in the reports on the project, either by the researcher or by any other party.

I understand that data and interview transcripts will be anonymised to prevent my identity from being made public.

I also understand that my participation is voluntary, that I am not under any obligation to answer questions and I can choose to participate in part or in full of the project and that I can withdraw from the project at any time I wish to without being penalised or disadvantaged in any way.

I consent to the processing of my personal information for the purposes of this research study. I understand that such information will be treated as strictly confidential and handled in accordance with the Data Protection Act 1998.

I also agree that the information obtained in this project can be used in further research projects which have research governance approval as long as any information that can be used to identify me or the organizations I am affiliated too is removed before it is passed on.

Name: ……

Signature……

Date:……..

University of Sussex

Participation information sheet- Healthy Volunteers

Title of research:

Risk, Reward and Regulation: Exploring Regulatory and Ethical Dimensions of Human Research Participation in phase I (first in man) clinical trials in the United Kingdom

What is the research about?

As part of my PhD (DPhil) studies at the University of Sussex I am carrying out a piece of research focusing on the regulatory and ethical aspects of first in man trials. I am particularly interested in finding out people's motivation for involvement in clinical trials, the role of financial rewards and their impact on the informed consent. Furthermore, I would like to find out if there are existing interest and advocacy organizations interested in voicing concerns for healthy volunteers and how presence or lack of such institutions impacts on the ethical practice of first in man trials.

This project and the researcher are independent of the clinical study you are taking part in and your involvement or findings of this study will not affect or jeopardize your arrangements or agreements with the organization that has recruited you to take part in the trial.

What will my participation involve?

There are two sides to your participation in this project:

1. Observations

With prior permission to the company running clinical trials, I will be observing you during the time you are taking part in the clinical trial. My observations will be focus on the processes and regimes that are in place for you during the time you are in this trial and not on your character or behaviour. I will also focus on the interactions between staff and volunteers. My observations will not be discussed with any of the company officials and will not in any way affect your present or future involvement in clinical trials with this company

2. Interviews

At the end or towards the end of the clinical study, the second part will be an interview with you. The interview will aim at discussing your opinions about your experience of involvement in clinical trial/s, your views about aspects of clinical trials such as decision making, availability of support networks, risks and benefits. You will choose when you want to be interviewed and how. Therefore, this would take a face-to-face conversation or a telephone conversation. We may also talk about your history of involvement in clinical trials.

3. After interview

I will transcribe the interview, which is to put the interview on paper. If you are willing, you will be able to review these texts and highlight anything you think was a misquotation or misinterpretation of your account.

How will the information shared in interviews be recorded?

With your permission, verbalised interviews (face to face or telephone interviews) will be audio recorded. Only the researcher will have access to them. It is possible that I will also take a few notes during the interview.

What will happen to the information I provide?

Together with the information gather during observations and interviews with other informants, the information you share may be used to inform my DPhil thesis and possibly published articles or conference speeches. In each case, anonymity will be ensured.

Anonymity and Confidentiality:

In accordance with the Data Protection Act, 1998, all research data, together with any personal information which may be collected during the research process, will be securely and anonymously stored in password protected files on a password protected system. All information will be destroyed once the research is completed.

Can I change my mind about participation?

Yes at any time you wish you can withdraw from participating, and if you decide that you do not want information that you already shared to be included in the research this will be done. You are free to with draw consent until such a time that this is no longer practical. If you wish to withdraw please contact me on sm388@sussex.ac.uk

If you have any further questions please do not hesitate to contact me: sm388@sussex.ac.uk or PG Pigeon Holes, Friston Building, University of Sussex, Brighton, BN1 9SP.

Shadreck Mwale

DPhil Candidate, Department of Sociology

University of Sussex

University of Sussex

Participation information sheet- Professionals from regulatory bodies

Title of research:

Risk, Reward and Regulation: Exploring Regulatory and Ethical Dimensions of Human Research Participation in phase I (first in man) clinical trials in the United Kingdom

What is the research about?

As part of my PhD (DPhil) studies at the university of Sussex I am carrying out a piece of research focusing on the regulatory and ethical aspects of first in man trials. I am particularly interested in finding out people's motivation for involvement in clinical trials, the role of financial rewards and their impact on the informed consent, risk perception and participation in clinical trials. Furthermore I would like to find out if there are existing interest and advocacy organizations interested in voicing concerns for healthy volunteers and how presence or lack of such institutions impacts on the ethical practice of first in man trials, and in turn explore the adequacy of current regulations in the provision of protection to UK citizens who volunteer in such trials.

What will my participation involve?

1. Interviews

Your involvement in this study will be an interview with you. The interview will aim at discussing your opinions about your experience of regulating in clinical trial/s, your views about aspects of clinical trials such as decision making, availability of support networks, risks and benefits and issues associated with regulation of first in man trials. You will choose when you want to be interviewed and how. Therefore this would take a face to face conversation or a telephone conversation. We may also talk about your history of involvement in clinical trial regulation in general.

2. After interview

I will transcribe the interview, if you are willing you will be able to review these texts and highlight anything you think was a misquotation or misinterpretation of your account.

How will the information shared in interviews be recorded?

With your permission, verbalised interviews (face to face or telephone interviews) will be audio recorded. Only the researcher will have access to them. It is possible that I will also take a few notes during the interview.

What will happen to the information I provide?

Together with the information gather during observations and interviews with other informants, the information you share may be used to inform my DPhil thesis and possibly published articles or conference speeches. In each case anonymity will be ensured.

Anonymity and Confidentiality

In accordance with the Data Protection Act, 1998, all research data, together with any personal information which may be collected during the research process, will be securely and anonymously

stored in password protected files on a password protected system. All information will be destroyed once the research is completed.

Can I change my mind about participation?

Yes at any time you wish you can withdraw from participating, and if you decide that you do not want information that you already shared to be included in the research this will be done. You are free to with draw consent until such a time that this is no longer practical. If you wish to withdraw please contact me on sm388@sussex.ac.uk

If you have any further questions please do not hesitate to contact me: sm388@sussex.ac.uk or PG Pigeon Holes, Friston Building, University of Sussex, Brighton, BN1 9SP.

Shadreck Mwale

DPhil Candidate, Department of Sociology

University of Sussex

University of Sussex

Participation information sheet- Professionals from Contract Research Organizations (CRO)

Title of research:

Risk, Reward and Regulation: Exploring Regulatory and Ethical Dimensions of Human Research Participation in phase I (first in man) clinical trials in the United Kingdom

What is the research about?

As part of my PhD (DPhil) studies at the University of Sussex I am carrying out a piece of research focusing on the regulatory and ethical aspects of first in man trials. I am particularly interested in finding out people's motivation for involvement in clinical trials, the role of financial rewards and their impact on the informed consent. Furthermore I would like to find out if there are existing interest and advocacy organizations interested in voicing concerns for healthy volunteers and how presence or lack of such institutions impacts on the ethical practice of first in man trials. I also want to find out about the interpretation and practical implementation of regulatory guidelines by CROs.

It is also important to stress that this project is independent of the CRO and your participation in this project will not be discussed with your employers neither shall it jeopardize your current or future employment.

What will my participation involve?

There are two aspects to your participation in this project:

1. Observations

With prior permission to the company running clinical trials I will be observing you during the time you are administering/supervising the clinical trial. My observations will be focused on the processes and regimes that are in place for you during the time you are administering this clinical trial and not on your character or behaviour. I will also focus on the interactions between staff and volunteers. My observations will not be discussed with any of the company officials and will not in any way affect your present or future employment with this company or any other

2. Interviews

During the course of the clinical trial there will be an interview with you. The interview will aim at discussing your opinions about your experience of administering in clinical trial/s, your views about aspects of clinical trials such as decision making, availability of support networks, risks and benefits, how you implement guidelines. You will choose when you want to be interviewed and how. Therefore this would take the form of a face to face conversation or a telephone conversation. We may also talk about your history of work in clinical research.

3. After interview

I will transcribe the interview, and if you are willing you will be able to review these texts and highlight anything you think was a misquotation or misinterpretation of your account.

How will the information shared in interviews be recorded?

With your permission, verbalised interviews (face to face or telephone interviews) will be audio recorded. Only the researcher will have access to them. It is possible that I will also take a few notes during the interview.

What will happen to the information I provide?

Together with the information gather during observations and interviews with other informants, the information you share may be used to inform my DPhil thesis and possibly published articles or conference speeches. In each case anonymity will be ensured.

Anonymity and Confidentiality

In accordance with the Data Protection Act, 1998, all research data, together with any personal information which may be collected during the research process, will be securely and anonymously stored in password protected files on a password protected system. All information will be destroyed once the research is completed.

Can I change my mind about participation?

Yes at any time you wish you can withdraw from participating, and if you decide that you do not want information that you already shared to be included in the research this will be done. You are free to with draw consent until such a time that this is no longer practical. If you wish to withdraw please contact me on sm388@sussex.ac.uk

If you have any further questions please do not hesitate to contact me: sm388@sussex.ac.uk or PG Pigeon Holes, Friston Building, University of Sussex, Brighton, BN1 9SP.

Shadreck Mwale

DPhil Candidate, Department of Sociology

University of Sussex

Appendix Two: Survey questionnaire

Questionnaire

Title: Healthy volunteer views and Experiences in First time-in-human clinical trials

Consent information

Purpose of the Study:

This questionnaire is part of a university of Sussex PhD research project on regulation and ethics in first-in-human clinical trials being conducted by Shadreck Mwale. One of the aims of this project is to document and collate views of healthy volunteers on their experiences with the hope of developing and understanding volunteer experience. To achieve this we would like to hear from healthy volunteers on their views on aspects of the clinical trial process.

Confidentiality:

Your responses will be kept completely confidential. Note that this research is for a PhD study at the University of Sussex and that your responses will **NOT IN ANYWAY disqualify you**, on the basis of your responses to this survey, from any future involvement in any clinical trial. However, it is being administrated by Richmond Pharmacology because they share an interest in improving relations with volunteers, with the intention of improving the volunteering experience.

Decision to quit at any time:

Your participation is voluntary; you are free to withdraw your participation from this study at any time. If you do not want to continue, you can simply leave this website. If you do not click on the "submit" button at the end of the survey, your answers and participation will not be recorded. You also may choose to skip any questions that you do not wish to answer. Should you wish to withdraw your responses after completing the survey from inclusion in the final report, you are free to do so until such a time that this is not practically possible. To withdraw from participation at any stage email s.mwale@sussex.ac.uk.

How the findings will be used:

The results of the study will be used for scholarly purposes only. The results from the study will be presented in educational settings and at professional conferences, and the results might be published in a professional journal in the field of Sociology and bioethics. Because we will ask you about a number of different aspects of volunteering in clinical trials, it is likely that we will use your data to address multiple questions regarding Healthy volunteer experiences.

Contact information:

If you have concerns or questions about this study, please contact Shadreck Mwale on s.mwale@sussex.ac.uk. By beginning the survey, you acknowledge that you have read this information and agree to participate in this research

Thanks in advance for your help and support.

Part 1- How you get involved

1. On a scale of 1-5 (1 being not useful at all and 5 very useful) please rate how useful the following are as sources of information about up-coming clinical trials for you? (select one box per row)

	Not useful at all	Not useful	Not sure	useful	Very useful
a. Network of healthy volunteer friends	1	2	3	4	5
b. Websites	1	2	3	4	5
c. Print media (newspaper or magazine)	1	2	3	4	5
d. Emails from Clinical Research Units	1	2	3	4	5
e. Other. Please specify	[Free Text]				

2. How many trials have you participated in since becoming a volunteer?

(Please give a number) ☐

3. Do you only take part in clinical trials run by a specific clinical trials unit, or do you go wherever there are studies recruiting? (please select one)

a. Yes ☐ b. No (Go to Q5) ☐

4. If you only volunteer for a specific Unit, on a scale of 1-5 (1=strongly disagree and 5= strongly agree) please state how strongly you agree or disagree with the following statements as reasons for doing so. (Please Select one per row)

	Strongly disagree	disagree	Not sure	agree	Strongly Agree
They pay good rates	1	2	3	4	5
I am familiar with staff	1	2	3	4	5
The facilities are good	1	2	3	4	5
Other (please state)	[Free Text]				

5. If you go to different units, on a scale of 1-5 (1=strongly disagree and 5= strongly agree) state how strongly you disagree or agree with the following statements as reasons why? (Please select one per row)

	1	2	3	4	5
I am likely to take part in more trials	1	2	3	4	5
The variation in rates paid means I choose where to get a good deal	1	2	3	4	5
Other reason please specify.....	[Free Text]				

Part 2 -Most recent involvement

6. Thinking about the most recent trial you took part in,

   A. How long ago was it? (Please select one choice only)

      i) Less than a month ☐

      ii) 1-3 months ☐

      iii) 4-6 months ☐

      iv) More than 6 months ☐

   B. How did you hear about it (select one choice only)

      i) Through friends ☐

      ii) Websites ☐

      iii) Text from research company ☐

      iv) Newspaper/magazine ☐

      v) Other please state[Free Text Box]…….

   C. How long did the trial last (including follow up days where appropriate? (select one choice)

      i) 1-7 days ☐

      ii) 1-2 weeks ☐

      iii) More than 2 weeks ☐

   D. Approximately how much were you paid?

      i) £100-£500 ☐

      ii) £501-£999 ☐

      iii) £1000-£1999 ☐

      ☐

iv) More than £2000

E. What was your employment status at the time? select any two that apply

I. Employed ☐

II. Employed Part-time ☐

III. Student Full-Time ☐

IV. Student Part-Time ☐

V. Not employed at all ☐

Part 3- Deciding to take Part

7. Thinking of the most recent trial you took part in, on a scale of 1-5 (1=strongly disagree and 5= strongly agree) state how strongly you agree or disagree with the following statements stating at what stage you decide to take part in any clinical trial? (select one box per row)

	1	2	3	4	5
After considering information about the trial and reward on offer	1	2	3	4	5
After consultations with family and friends	1	2	3	4	5
After receiving further information about the trial during admission	1	2	3	4	5

8. On a scale of 1-5 (1 being least important and 5 being very important) please rate how you consider the following to be important for you before deciding to take part in a clinical trial? (Please select one box per row)

	1	2	3	4	5
how the trial dates fit into my work schedule	1	2	3	4	5
The monetary compensation on offer	1	2	3	4	5
How long you have to stay in the unit	1	2	3	4	5
How many follow up visits you have to make	1	2	3	4	5
The potential risks involved in the trials	1	2	3	4	5

Which unit is carrying out the study?	1	2	3	4	5
The perceived level of discomfort you may have to endure	1	2	3	4	5

9. Thinking about the most recent trial you volunteered in, on a scale of 1-5 (1 being very unsatisfied and 5 very satisfied) how do you rate your satisfaction with the information given to you regarding the benefits and possible risks of the trial? (Please select one)

Very unsatisfied	Unsatisfied	Did not bother me	Satisfied	Very Satisfied
1	2	3	4	5

10. In generally on a scale of 1-5 (1=strongly disagree and 5= strongly agree) state how strongly you agree or disagree with the following statements as reasons for volunteering in clinical trials. (Please select one box per row)

	1	2	3	4	5
The monetary compensation on offer is important in my decision to take part	1	2	3	4	5
The purpose of the potential drug was important in my decision to take part	1	2	3	4	5
The desire to help in the advancement of science is important in my decision to take part	1	2	3	4	5
To help in the development of drugs that could potentially save lives	1	2	3	4	5
Other (please state).....	[Free Text]				

11. Imagine you were sent a text/sms about a trial that needed participants urgently. For each of the following statements please indicate your likelihood of taking part in a trial on a scale of 1-5. (1 being Extremely unlikely and 5 Extremely likely) (select one box per row)

	1	2	3	4	5
1. If paid £1000 for 5 day , 5 night stay in a trial I would take part	1	2	3	4	5

2. I would still take part if paid £200 for a 5 day, 5 night stay	1	2	3	4	5
3. I would take part even if it has been less than 4 weeks since my last trial	1	2	3	4	5
4. If paid £1000 for a 5 day overnight stay I would take part despite the potential risks of the trial	1	2	3	4	5
5. Payment is not important for me, I would still take part	1	2	3	4	5

12. As part of the study I would like to talk in more detail with some healthy volunteers in a brief interview. Would you be willing at your convenience to take part in a confidential interview? In return you will be given a £20 Amazon voucher.

    a. Yes ☐ b. No ☐

13. If so, please provide your contact details (**email or Phone number**) so this can be arranged

…….

ABOUT YOURSELF

14. What is your age category

    a. 18-21 ☐
    b. 22-29 ☐
    c. 30-40 ☐
    d. 41+ ☐

15. Gender

    a. Male ☐
    b. Female ☐

16. What is your highest level education qualification (please select one)

    a. Degree or higher degree ☐
    b. Higher educational qualification below degree level ☐
    c. A levels or Higher ☐
    d. ONC/BTEC ☐
    e. O level ☐
    f. GCSE ☐

☐

g. Other qualifications (inc foreign qualifications below degree level)

h. No formal qualifications ☐

i. Don't know ☐

17. Apart from volunteering in clinical trials are you (Please select one or fill in accordingly)

a. Employed full time ☐

b. Employed Part-time ☐

c. unemployed ☐

d. if you are employed please state your occupation (i.e. Teacher; plumber……)[FREE TEXT BOX]

e. if you are unemployed/employed are you

1. Full-time Student ☐

2. Part-time student ☐

3. None of the above ☐

18. If you are employed, how much is your annual income (select one)

a. Less than £10,000 ☐

b. £10,000-£15,000 ☐

c. £16,000-£20,000 ☐

d. More than £21,000 ☐

e. Prefer not to say ☐

19. How would you describe your marital status (Select one)

a. Married ☐

b. In a relationship but not married ☐

c. Single ☐

d. Widowed ☐

e. Divorced ☐

20. Do you have any dependants

Yes ☐ No (Go to Q 22) ☐

21. If yes how many dependents do you have? (State number) .....

22. How would you describe your ethnicity (Please select one or write where appropriate)

Asian-Japanese ☐

Asian Chinese ☐

Asian Pakistani ☐

Asian Indian ☐

Other Asian please specify…[FREE TEXT BOX]

Black African ☐

Black Caribbean ☐

Mixed ☐

White Caucasian ☐

Other Ethnic group please specify...[FREE TEXT BOX]

23. How would you describe your nationality (Please select one and/or write accordingly)

a. British national ☐

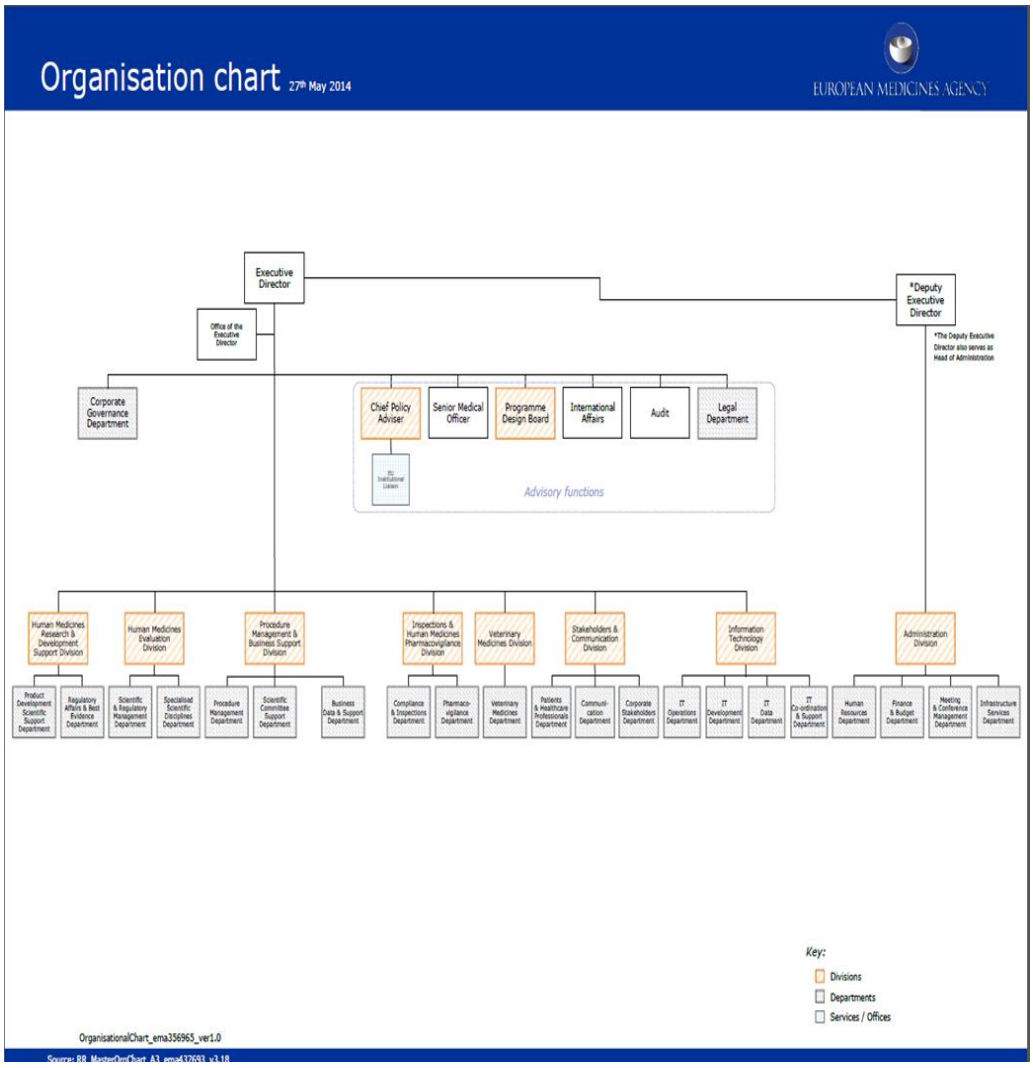
b. British Resident but EU national (Please state country) ☐

c. EU national Resident in an EU Country (please state country) ☐

d. British Resident but of other nationality (please state country) ☐

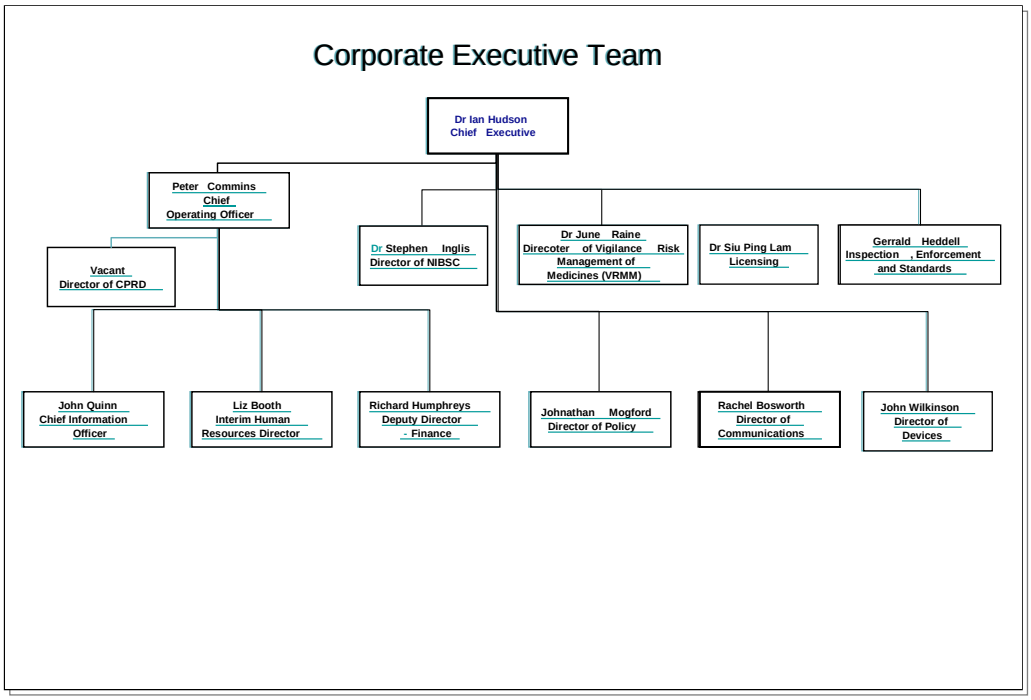
Thank you!

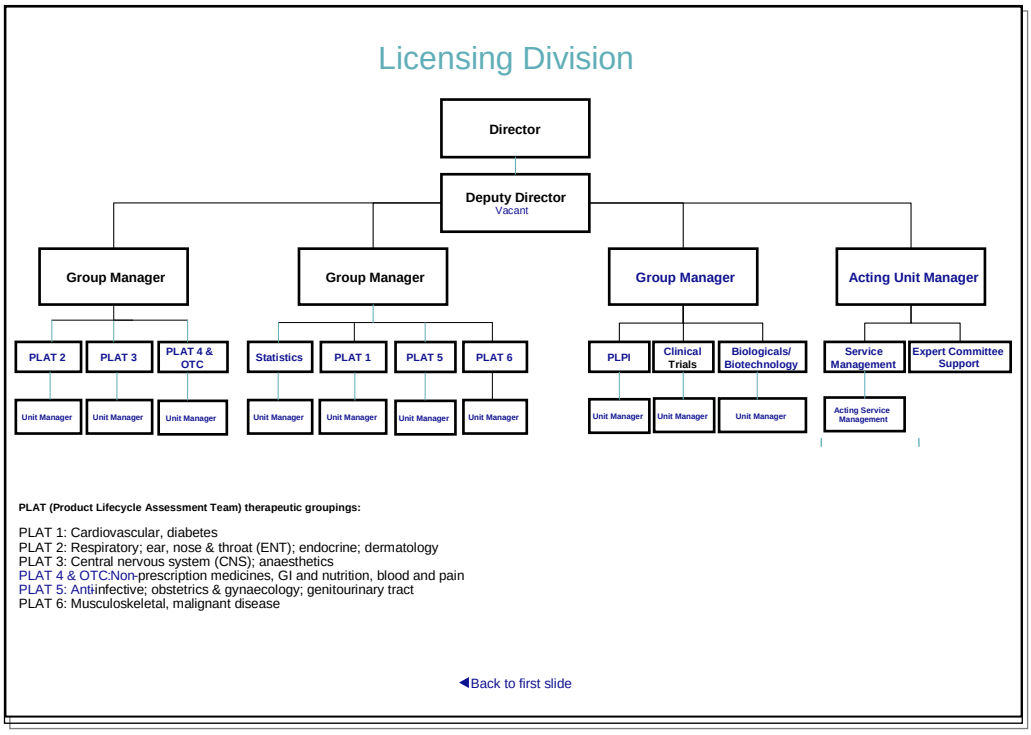
Appendix Three: Organisational Charts- For EMA and MHRA



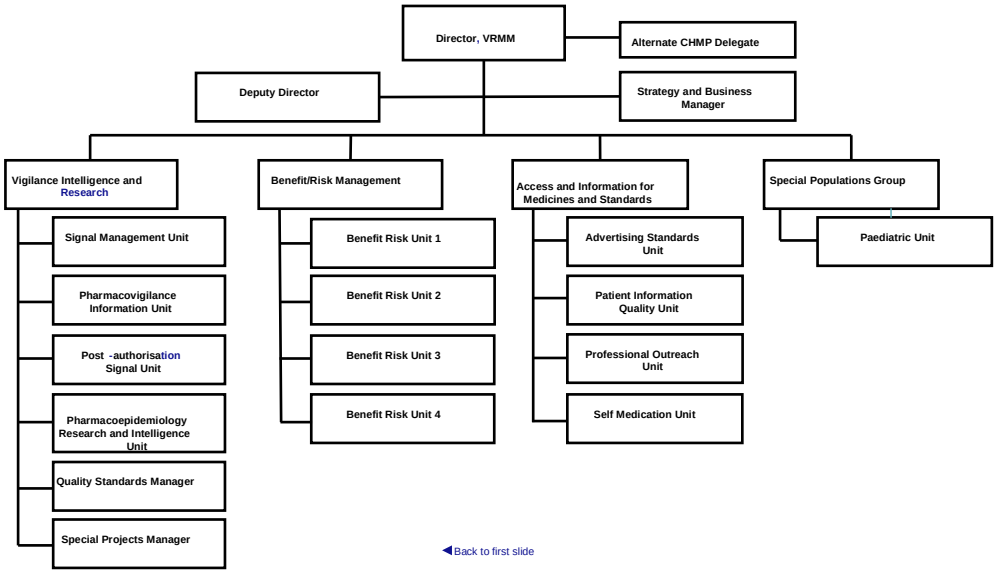
Organisational and (Some)Divisional Charts of the MHRA

source: http://www.mhra.gov.uk/Aboutus/Ourstructure/Organisationchart/index.htm





Vigilance Risk Management of Medicines (VRMM)



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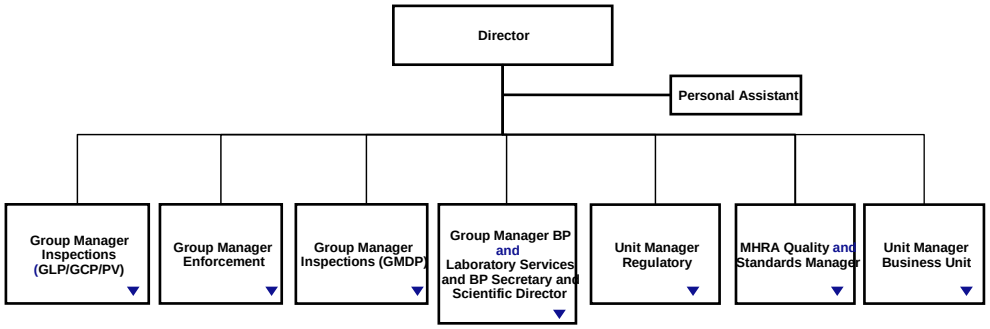
Inspection, Enforcement and Standards (IE&S) Division



GLP – Good Laboratory Practice
GCP – Good Clinical Practice
GDP – Good Distribution Practice
PV – Good Pharmacovigilance Practice
WGC - Welwyn Garden City
BPR – Buckingham Palace Road
Y - York

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Appendix Four- Ethics approval certificates

University of Sussex

Social Sciences Research Ethics Committee CERTIFICATE OF APPROVAL	
Reference Number:	1112/12/08
School:	LPS
Title of Project	Risk, Reward And Regulation: Exploring Regulatory And Ethical Dimensions Of Human Research Participation In Phase I (First In Man) Clinical Trials In The United Kingdom
Principal Investigator: (Supervisor as applicable)	Shadreck Mwale (Prof J Abraham)
Expected Start Date:*	01/02/2012

*NB. If the actual project start date is delayed beyond 12 months of the expected start date, this Certificate of Approval will lapse and the project will need to be reviewed again to take account of changed circumstances such as legislation, sponsor requirements and University procedures

This project has been given ethical approval by the Social Sciences Research Ethics Committee (C-REC). ***Please note the following requirements for approved submissions:***

Amendments to research proposal - Any changes or amendments to the approved proposal, which have ethical implications, must be submitted to the committee for authorisation prior to implementation.

Feedback regarding any adverse and unexpected events - Any adverse (undesirable and unintended) and unexpected events that occur during the implementation of the project must be reported to the Chair of the Social Sciences C-REC. In the event of a serious adverse event, research must be stopped immediately and the Chair alerted within 24 hours of the occurrence.

Authorised Signature	
Name of Authorised Signatory (C-REC Chair or nominated deputy)	Dr Elaine Sharland 12/01/2012

University of Sussex

Social Sciences Research Ethics Committee CERTIFICATE OF APPROVAL	
Reference Number:	1112/12/08 (As amended)
School:	LPS
Title of Project	Risk, Reward And Regulation: Exploring Regulatory And Ethical Dimensions Of Human Research Participation In Phase I (First In Man) Clinical Trials In The United Kingdom
Principal investigator (Supervisor)	Shadreck Mwale (Bendelow/Faulkner)
Date of project:	February 2012 – May 2013
*NB. If the actual project start date is delayed beyond 12 months of the expected start date, this Certificate of Approval will lapse and the project will need to be reviewed again to take account of changed circumstances such as legislation, sponsor requirements and University procedures	
This project has been given ethical approval by the Social Sciences Research Ethics Committee (C-REC). ***Please note the following requirements for approved submissions:*** **Amendments to research proposal -** Any changes or amendments to the approved proposal, which have ethical implications, must be submitted to the committee for authorisation prior to implementation. **Feedback regarding any adverse and unexpected events -** Any adverse (undesirable and unintended) and unexpected events that occur during the implementation of the project must be reported to the Chair of the Social Sciences C-REC. In the event of a serious adverse event, research must be stopped immediately and the Chair alerted within 24 hours of the occurrence.	
Authorised Signature	Stephen Shute
Name of Authorised Signatory (C-REC Chair or nominated deputy)	Professor Stephen Shute 11/02/13