

Testing Pills, Enacting Obesity

The work of localizing tools in a clinical trial

Petra Jonvallen

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Clinical trials and the problem of obesity

*As my journey through the pharmaceutical jungle progressed, I came to realize that, by comparison with the reality, my story was as tame as a holiday postcard.
("author's note" in John Le Carré's *The Constant Gardener*, 2001)*

The multinational pharmaceutical industry is surrounded by drama and controversy. Murky fictional and factual tales are told about pharmaceutical companies using sick people in pursuit of their own profit, often in a conspiratory genre. John le Carré's bestselling novel dramatically describes how sinister pharmaceutical actors conduct poorly controlled clinical trials of a tuberculosis medicine on powerless patients in Kenya and then hide evidence of the deaths that occur as a result. A non-fictional example can be seen in an essay on the Culture pages in the largest Swedish daily paper, *Dagens Nyheter*, in February 2002, where a former sales manager in the pharmaceutical industry showed with real-life examples how money always goes before morale under the heading "Pharmaceutical companies sell useless pills" (Hägglöf 2002). Parallel to these negative images of the industry are the hopeful expectations of the industry's role in finding solutions to serious diseases and health problems, and (perhaps even more) of the jobs the industry will provide and its importance to the economy as a whole. In this study, I will not attempt to answer to what extent such images reflect reality, but provide a better understanding of the conditions under which the pharmaceutical industry operates, the mechanisms guiding its production processes, and in so doing, demystify *how* the industry does what it does.

This dissertation focuses on one specific area of interest to the pharmaceutical industry: large scale clinical trials on obesity drugs. The obesity population figures have received immense and increasing amounts of attention during the last decades due to the indisputable fact that more and more people in "westernised" parts of the world are becoming measurably heavier. In Sweden, a country with a population just over 9 million, around 575,000 people

were categorized as obese¹ in the beginning of the millennium, and obesity is often claimed to be one of the fastest growing health problems on a national and international level (Kallings 2002). Biomedical research has shown that obesity has a direct relationship to diseases such as type 2 diabetes, hypertension and heart disease which cause high costs for already strained national health care budgets. This has led the World Health Organisation to label obesity a global epidemic (WHO/NUT/NCD/98) and a number of actors have mobilised forces to fight the metaphorical war on body fat. Obesity researchers are trying to find a cure and the food industry is marketing healthier food, to name but a few measures. The global pharmaceutical industry is perhaps the most powerful actor when it comes to this “trillion dollar disease”, as one science journalist calls it (Shell 2002). It is currently in the process of trying out a considerable number of new obesity drugs in a multitude of places worldwide.

More specifically, this dissertation focuses on the clinical trial phase of pharmaceutical production, and even more specifically, a so called phase III clinical trial. Such a trial involves thousands of participant volunteers and hundreds of hospital clinics worldwide. It is rightly often referred to as ‘the clinical trial business’, considering the sums invested in the research, development and marketing of obesity drugs. In this study I describe in detail the everyday work and tools involved in a large scale, industry sponsored, clinical drug trial, something that has not been done from a social science perspective before².

The overarching objective of this study is to gain increased knowledge about the kinds of work involved in large scale clinical trials. By means of fieldwork consisting of observations, semi-structured interviews (with those working with the trials, not the participants themselves) and analysis of written material I focus on the local practices and discourses of one large scale clinical trial with its local categories and contradictions. The pharmaceutical

¹ The etymological equivalent for “obese” and “obesity” in the Swedish language is *obes* and *obesitas*, respectively. These are the medical terms used by obesity researchers themselves. In everyday language the terms *fetma* and *övervikt* (fatness and overweight, respectively) are used. The colloquial *fetma* has somewhat derogatory connotations but has become used more frequently to denote the condition as a disease. The clinical staff in this investigation used both terms. *Övervikt* is a more general term which can include both minimally and extremely overweight persons. The Swedish association for obesity is named *Överviktigas riksförbund*, perhaps to avoid the, for many, derogatory term *fetma*. In comparison, The North American Association for Fat Acceptance, NAAFA, use the term ‘fat’ as a way to change its derogatory meaning. Swedish clinical staff can be seen as using the term ‘fetma’ in a similar way, to rid it of negative meanings, or neutralize it. Throughout the book, it is the medical definition of obesity that I use.

² Löwy (1996), Meuller (1997) and Epstein (1996) have studied clinical trials but have not focussed specifically on the relationship between tools and practice in clinical practice.

industry is highly involved in medical research (Goodman 1998). When it comes to relatively new disease areas, such as obesity, it is interesting to see in which way the industry affects how obesity is taking shape as a medical problem. I therefore also focus on the ways in which obesity, seen as a medical condition in the making, is enacted by the clinical trial staff.

Innovation processes, like those leading to new pharmaceuticals, have received much attention from economists and management researchers. They mainly focus on issues such as market competition, state regulation and firms' strategies to increase profit (i.e. Bergenheim 2000, Gassman et al. 2004). But, to understand the complexity of a clinical trial as a site where private industry meets public health care, an economic or management perspective is not enough. Attention must also be given to cultural or social processes, the interrelations and practices involved in clinical trials. Studying clinical trials is therefore a good chance to link the economic and cultural sides of the social sciences, as Van der Geest et al. have pointed out:

Pharmaceuticals constitute a perfect opportunity for the study of the relation between symbols and political economy. On one hand, they are a part of the international flow of capital and commerce. On the other, they are symbols of hope and healing and of the promise of advanced technology.

(Van der Geest et al. 1996: 170)

In this dissertation I have seized the opportunity to study the relationship between the terms of production of the pharmaceutical industry and what obesity "is" or means to the local actors in the context of clinical trials.

This work has two main themes. The first theme, *testing pills*, concerns the pharmaceutical production process itself, whereas the second theme, *enacting obesity*, is concerned with medical and social scientific descriptions of obesity and the medicalisation of body weight. First, and connected to the first theme, the concepts of a randomized controlled trial (RCT) are introduced and some critiques of the method presented. Then, the technoscientific character of clinical trials is highlighted in order to pinpoint why a focus on tools is important. Finally, the so called science/care dilemma in clinical research is introduced, as is the role of industry in the clinic. The second part of the chapter relates to the dissertation's second theme and provides the background necessary for understanding how obesity is enacted in the situated work practices involved in clinical trial work. In it, medical and social scientific research on obesity is briefly introduced, as are a selection of different views on the medicalisation of body weight.

Testing pills

Producing a pharmaceutical drug is a long and costly process that can take up to fifteen years to complete. Before clinical trials are performed, the substance has gone through extensive pre-clinical trials. The number of clinical trials has increased substantially during the last couple of decades and not many drugs that reach the market are new substances. Many of the clinical trials that are performed are done on existing substances, tested on new indications. In such cases, like the one studied here, clinical trials are performed against this new indication, where a former side effect is made into a main effect.

Clinical trials are often said to have beneficial consequences to the participant-patients, for whom they imply greater access to treatment. In a small and recently institutionalized part of the health care system such as obesity care, this argument is often forwarded (interview Markus)³. Being a participant in a clinical trial on an obesity pill is, for many, the only way to get health care for being medically defined as obese. Thus, and as Epstein has pointed out, the social meaning of clinical trials has changed from being one of research to being one of care (Epstein 1996: 197). Where there are no treatments, participation in clinical trials may be the only method of access to treatment.

Clinical trials have expanded into a veritable industry both in terms of the size of the trials, and in terms of the scope of the trials to test new conditions. The number of people taking part in clinical trial activities are many: for example, and as I will discuss later in this dissertation, during one month in Sweden in 2001, around 40,000 overweight and obese Swedish individuals made calls to register their interest in participating in the testing of a new drug against obesity. Out of these, only around 500 were enrolled in the trial. The remaining people could, however, choose to remain in the database constructed for this purpose, which would allow them to try to get enrolled in subsequent trials.

The gold standard

The randomized controlled trial is the predominant and most authoritative method whereby medical therapies are evaluated. In an RCT, participants are randomized into different “treatment arms”, where each group except one receives different strengths of the substance or other therapy tested. These are then compared with the remaining group which gets a non-

³ The names of those interviewed are pseudonyms. See chapter four.

active substance or placebo pill. In other words, the substance on trial is “controlled” against a placebo.

RCT’s are often referred to as being the gold standard in therapeutic evaluations. It became established as a standard shortly after the Second World War (Marks 1997). This process was contemporary to large scale organizational changes in biomedical research in Western Europe and the United States. Health care in the post-war period was becoming increasingly financed through state funding and a large scale care and research apparatus – “Big medicine” – became established. The public funding of health care and research also made it more sensitive towards criticism from the outside. Scientifically objective judgements and measurements through statistics served as protection for the clinical environment against eventual criticism of its practices. Clinical trials with statistically measurable objectivity fitted well into this new scenario. Scientific objectivity thus stood against the personal clinical experience of the doctor, and objectivity ‘won’. Such issues laid ground for the establishment of the RCT as a gold standard (for a more detailed historical analysis of this process see Marks 1997).

From the 1970’s and onward, critical voices began to be raised against how RCT’s were designed and conducted, as well as against the results. One significant event that opened up for such critiques was the thalidomide scandal in the 1960’s, when a drug to reduce morning sickness in pregnant women resulted in a large number of birth defects of the babies that were born. At the same time, influential researchers gave voice to a view deeming much of contemporary medical practice if not harmful, then ineffective (Pope 2003: 270). Those critical towards the clinical trial methodology claim that RCT’s are modelled on artificial experimental situations, which makes it impossible to answer questions emanating from everyday clinical situations. Instead, critics support different methods that, to a greater extent, emanate from doctors’ clinical judgements.

A more radical critique put forward against the RCT’s is that they can be seen as a tool that substitutes for moral or political decisions. Behind such a critique lies the view that it is not progress in scientific medicine that has led to the great improvements in health, cures for disease and life expectancy, but rather broader changes in society, such as socioeconomic development, better hygiene, better food and other factors related to the environment (see e.g. Illich 1976).

Another problem with there being a gold standard for assessing medical therapies is that the results of other investigations are deemed less scientific in comparison. Within the medical community, as in other communities, some accounts are more authoritative than

others. The epistemological authority of quantitatively based research such as the RCT has been seen to silence knowledge produced in other medico-scientific practices (Adams 2002, Jadad 1998, Marks 1997). Also, large scale research is, often explicitly, more authoritative than for example smaller case studies using qualitative methods. In a Swedish literature review of medical research on obesity treatments, for instance, the studies investigated were graded on a four grade scale of “evidence strength” (SBU report 2002). For a study to be granted high evidence strength the participants should, for example; be randomized, the number of study participants high, and the drop out rate low. Such studies require substantial amounts of funding – funding that is easier to get for pharmaceutical drug studies than for non-drug studies. Therefore, pharmacotherapy has a considerable lead as compared to less well documented therapies. Evidence from other therapeutic evaluations is seen as having low evidence strength. Thus, there is a connection between the increased prestige and power of biomedical researchers and the success of RCTs. One way to view clinical trials, in line with such an argument, is that that they, with their alliances of biomedical researchers, clinical researchers and pharmaceutical companies, consolidate the prestige and increase the control that research doctors have over those who do not do research, i.e. clinicians (Löwy 1996: 53).

The technoscientific nature of medical work

This research project is situated within the interdisciplinary field of science, technology and society studies (STS), which analyses science and technology as parts of society, where the former both shape, mirror, and are shaped by the latter (i.e. Bijker, Hughes and Pinch 1987, Latour 1987, Wajcman 1991). More recently, one subfield of this research has examined technology as having an important role in medical work (Berg 1997, Berg and Mol 1998, Clarke et al 2000, Johnson 2004, Mol 2002, Star 1995, Thelander 2001). These have taken seriously the technology used in medical practices.

In a recent article, Berg and Timmermans argue the need for an approach they refer to as technology-in-practice. Technology-in-practice is a synthesis of the previous two dominant paradigms of technological determinism and social determinism. Both can be avoided, they argue, if technology is studied in action rather than being either overestimated or underestimated (Berg and Timmermans 2003). This approach, inspired by actor network theory, places technology at the same level of analysis as human actors. Medical technologies are thus constituted by others and in turn constitute the actions of others (Ibid: 104).

Clarke et al. stress the centrality of technoscience in how hospitals, clinics and research are shaped. The incorporation of technoscientific innovations such as ICT's, databanks, advanced diagnostic tools and computerisation has large consequences for the practices and organisation of biomedicine. The innovations, they continue, are of a kind and scale that they imply a reconstitution of the whole biomedical domain, a "technoscientific revolution", similar to the industrial revolution (Clarke et al. 2000: 2). Part of this revolution is the use of computer based visualisation technologies, evidence based medicine and an increasingly computerised pharmaceutical production process. In the words of Clarke et al.:

Within the framework of the industrial revolution, we became accustomed to "big science" and "big technology" – projects such as the Tennessee Valley Authority, the atom bomb, even electrification and transportation grids. In the technoscientific revolution, "big science" and "big technology" sit on your desk or in a pillbox. (Clarke et al. 2000: 4)

The view of medicine in such a framework is that of a dynamic process involving the interactions of more than just medical staff, patients and hospitals. It also encompasses actors outside of the traditional medical arenas such as "lay people, corporations, government bureaucracies, drugs, devices, and technologies of many kinds, and involving a variety of competing knowledges, political and economic interests and large scale organizations at work" (Ibid. 8).

The importance of technoscience in medical practices will be a recurring theme throughout the study, and will be especially addressed in relation to the computer control system and clinical research protocols used in the clinical trial. In the long and costly technoscientific production of pharmaceuticals, of which a RCT is but one part, I have distinguished two central themes that that need further investigation. The first is the science/care dilemma which I will study as it is expressed in a local situation. Secondly, I have focused on the connections and boundaries between private industry and medical work.

The science/care di lemma

The RCT became pervasive since it was one important step in the process to base clinical decision-making on scientific objectivity rather than on clinical judgement, a process related to the movement of evidence based medicine. Knowledge grounded in clinical experience and clinical judgement is a type of knowledge often termed experience based knowledge. Such knowledge is regularly contrasted to more formal scientific knowledge. According to Marks,

who has written a history of clinical experimentation, the status of experience based knowledge has changed over time (Marks 1997). Early clinical trials incorporated clinical judgement in the trial design as well as in the conclusions drawn from the trial. It was the traditional base for a medical doctor's expert knowledge. Later clinical trials do not leave the same space for this type of knowledge, according to Marks.

The medical elite, which historically has legitimated its status through clinical expertise, promoted a method whose goal it was to lessen the significance of individual doctors' judgement based on the same expertise. One example of this shift from experience based knowledge to scientific knowledge in clinical experimentation is the increasing use of statistics in post-world war II medicine to achieve objectivity.

The relationship between clinical experience and scientific evidence is an often recurring theme in medical literature as well as among social scientists studying medical practices. It is a relationship often deemed full of tensions. How can scientific evidence be applied to individual patients when the clinical "reality" often does not match the presuppositions made by science? This tension is perhaps most evident in clinical trials, where the production of reliable evidence becomes directly intertwined with the care of the patient. Clinical research has been shown to blur the borders between what is seen as medical research and medical practice (Fox 1959/1974). The doctor or investigator tries out substances whose effects are not known, while simultaneously seeing to the health and illness related needs of the patient. Fox has studied how clinical researchers solved upcoming problems in the nexus of treatment and research, while at the same time negotiating the double roles that ensued. A conclusion that can be drawn from Fox's study is that clinical research to some extent undermines the structure and normative role of the doctor-patient relation. This undermining is something that contributes to new norms and values becoming institutionalised, which in turn contributes to the shaping of medical health care practice.

Mueller, who has studied the medical division of labour in clinical research, claims that doctors in certain cases work exclusively with background work such as formulating research problems, applying for funding and evaluating research results, while the clinical research tasks are performed increasingly by nurses (Mueller 1997: 57). Earlier clinical research, she continues, took place in hospital wards where doctors had an active role in the experimental procedures. Today, there are more specialised hospital wards where studies can be conducted, and several studies are conducted with patients living at home. The implementation and coordination, however, is often done by trial nurses. The implications and consequences of such an increase of nurses involved in clinical research, in combination with the decrease of

research doctors' clinical work, has been of interest to few, according to Mueller. She relates the entrance of nurses into clinical research to the decrease in status of clinical work tasks in relation to scientific medicine.

The contradictions within knowledge based care, or between research and care, are what Mueller refers to as the science/care dilemma, and expressed in several ways. One way is in the differences in how doctors and nurses view the patient (Ibid: 67). In Mueller's study, doctors primarily saw patients as participants in a research project, who were primarily valued through their contributions to broader clinical-scientific goals. To a lesser extent, the doctors saw them as patients in need of care, the perspective of the nurses. The ethical issues raised in medical ethics committees where clinical trials are evaluated often concern objectification of the patient as research objects. For the nurses, on the other hand, the clinical research protocol was not just a statistical tool, but rather part of the care of the patient in which the patient's advances and setbacks could be followed.

Difficulties in separating the role of care giver from that of the researcher are also pointed out by Oakley (1990). In her study, the midwives involved in clinical trials were actively involved with the patients and were often worried that the patients' needs had to give way to research interests. She shows how midwives in some cases tinkered with the randomization in order to make sure that the patients got the treatment they saw as best suited for their clinical needs.

The character of clinical trials is thus ambiguous in that it oscillates between being part of health care and between being part of clinical research. An indication of this is provided in the following excerpt, taken from a brochure aimed at clinicians about a course to learn the basics of doing clinical trial research.

Our patients are to be offered a knowledge based care. The knowledge is carried by our staff, and has to be renewed continually. Therefore, staff has to seek both old and new knowledge. It not only has to be understood but also accepted and implemented. Being active in research and development (R&D) is one part of forwarding this process. One form of R&D is clinical trials.

According to this description, the patients are to be offered knowledge-based care, and clinical trials are conceptualised as a part of this goal. Clinical trials are further defined as a form of research and development. This line of reasoning can be seen as part of a broader effort to dissolve the dichotomy of research and care, and thus in a way an attempt to solve the science/care dilemma.

This attempt is in line with a larger movement within medicine that goes under the term evidence based medicine. It can be seen as a movement critical of medical knowledge production based only on clinical judgement only, without using existing scientific evidence in deciding what to do in the clinical situation. According to Pope, evidence based medicine can be characterized as a social movement with proponents and resisters. These can be organized under what the evidence base of medicine is thought to be by its different actors, what Pope calls rational/technical or contingent/experiential. To its resisters, evidence based medicine, epitomized by the RCT, presents a “threat to clinical judgement’ in that it privileges the rational/technical aspects of medical work over the contingent/experiential (Pope 2003: 278).

Industry in the clinic

Connections between the medical research community and pharmaceutical industry are tight and many. These are connections that lead to much fruitful cooperation, but also to conflicts. Recent research has focussed on the cooperation between science, industry and government, where terms such as the “new production of knowledge” (Gibbons et al. 1994) and “triple helix” (Leydesdorff & Etzkowitz 1996) are used to pinpoint a new state of affairs. This research, however, does not see to the local actors and local practices, i.e. how each part of the helix is visible for or constructed by the different actors in actual and local settings.

One problem brought about by the tight connections between medical practitioners and industry is the significant influence of industrial interests on public health care and research. This influence means a potential and often acclaimed threat to medical discretion and autonomy. New research cultures are said to have arisen through new cooperations between scientists and industry. In Varma’s study of research cultures in high technology industries, she finds some clear tendencies of such change: research has become business rather than science driven, consumers’ needs are in focus already at the research stage, and persons involved in research projects are to an increasing extent non-scientists. Also, basic research has decreased in relation to development research, something that makes it difficult to distinguish between the two categories. Academic research is also increasingly valued on the basis of what it can contribute to industry, in terms of commercialisation, cost efficiency and profit, rather than in terms of its technical or scientific contribution. There are more and more instances of outsourcing of research to countries with cheaper labour costs, and of information

flows outside traditional communication structures. Last but not least: the funding increasingly comes from private rather than public sources (Varma 2000).

As to whether such changes are good or bad, opinions differ. For the individual researcher, it opens up a broader range of career possibilities, something that also implies that researchers to a greater extent than previously have to take into consideration the “broader implications” of research (Varma 2000: 413). The problem with these developments is that it may not be an ethos of scientific knowledge that decides the work of a scientist but perhaps rather conformity to industrial interests. These are implications that may well be in conflict with the public interest. Abraham for instance shows that a scientific document can become entangled in a conflict between public and industrial interests, which do not always converge. The pharmaceutical companies, for instance, may wish to overemphasise the effectiveness of a drug, but minimise publicity of its toxicity (Abraham 1995).

Industry is also visible in the clinic through its simultaneous development and marketing of a drug. Clinical trials can be seen as part of the marketing strategy of pharmaceutical companies. Oudshoorn (1994) sees the clinical trials which tested sex hormones in the 1920's and 1930's as a marketing device. The benefits of taking hormones were difficult to explain to potential users, and organizing clinical trials was part of a strategy of informing future users/patients about the therapeutic value of the treatment.

Oudshoorn also shows how clinical trials were important tools for the bringing together of pharmaceutical companies and medical professionals. The trials enabled the pharmaceutical firm to “cultivate a loyal clientele in the medical profession”, which in turn ensured close ties to its market (Oudshoorn 1994: 108). The relationship between pharmaceutical entrepreneurs and medical researchers, she shows, was beneficial to both. Both gynaecologists and pharmaceutical entrepreneurs had interests in the marketing of female sex hormones as “scientific drugs” since it helped establish the scientific status of both groups. “In the striving for a scientific image, the clinic and the pharmaceutical industry matched each others' needs, a process in which female sex hormones became of mutual interest and gradually developed into big science and big business” (Ibid: 109).

With such a perspective, the researchers and research subjects in clinical trials have additional roles of being, respectively, producers and consumers of pharmaceutical drugs. The amount of diagnoses increase as the amount of available drugs increase, something that has been referred to as “the diagnostic bracket creep” (Kramer 1993: 15, in Fishman 2004), meaning that diagnostic criteria are loose enough to allow for high levels of diagnoses and a tendency for doctors to prescribe a particular drug for an ever-widening circle of symptoms.

And, as the number of diagnoses increases, so does the market. In fact, companies make efforts not only to market a pill, but also to market the medical condition itself. A discussion of what is a disease treatable with pharmacotherapy is noticeable in medical journals, such as in a debate article in *British Medical Journal* in 2002 where such a phenomenon has been referred to as “corporate backed disease mongering” (Moynihan, Heath & Henry 2002). Thus, the borders for where research and development ends and marketing starts are blurry.

Clarke et al. argue that there are processes of increasing corporatization of previously funded state tasks and a commodification of the knowledge previously produced by state employees. The term Biomedical TechnoService Complex™, Ltd. that they use connotes the state of affairs in the domains of health and illness with emphasis on its “profound corporatization and privatized commodification” (Clarke et al. 2000: 14). This corporatization and commodification, implies an implosion of categories such as public and private, patient and consumer, as well as university and industry, even though these processes are different in different national contexts. Nevertheless:

[...] private corporate entities seek to appropriate increasing areas of the health care sector under private management and /or ownership. That is, the frontiers of what is legitimately defined as private as opposed to public medicine, corporatized versus non-profit medicine are expanding and being reconfigured. (Clarke et al. 2000: 20)

The extent to which processes of commodification and corporatization are prevalent in the Swedish medical context is likely to be different, even if some characteristics are similar. The Swedish health care system is not nearly as corporatized as in the USA, for example, but has had a trend of increasing corporatization in the last decade.

Private industry’s involvement in public health care and clinical research has been seen as problematic in a number of ways. It is sometimes perceived as a threat to medical discretion and autonomy, and as making research business rather than science driven. The process of increasing corporatization is also seen as causing blurry boundaries between private and public. Such reasoning has led to questions about whether the patient is a patient or a consumer and if it is problematic if he/she is both. The character of the relationship between private entities and the clinic when it comes to Swedish clinical practices is a matter that deserves investigation, as well as the ways in which boundaries between public and private and patient and consumer are being reconfigured. I will analyse how the configurations of industry and care are expressed in the local and everyday work of the clinical trial.

Enacting obesity

The second theme of this dissertation is the medically defined condition of obesity, the very background to the production of obesity pills. The technology-in-practice approach means not taking any actor or phenomenon as a given, but instead examining how it is constituted in local practice. The object being tested, the obesity pill, and indeed obesity itself, will also need to be analysed.

There are different views on what obesity is, depending on which perspective is used to analyse it. Medical research and social scientific research have different perspectives of what obesity is, for example. This research will be shortly reviewed, and a selection of different actors' views on the obesity problem will be introduced. This contextualisation is necessary before it is possible to do an analysis of how obesity is enacted in the specific clinical trial in focus in this book: the Obe trials. Through such a background, issues not raised by informants in the local setting, but nevertheless important, can be included in the analysis. The background is also important in order to understand the circumstances under which obesity drugs are developed.

Medical and social research on obesity

In clinical and epidemiological studies, obesity is defined in terms of the amount of body fat a person has. There is ample evidence that an increased body mass index⁴ can be correlated to increased risk of death (WHO report). Obesity is an increasing health problem, but the extent to which this is so differs between different population groups. In the Swedish middle-aged population group, the prevalence of obesity (defined as body mass index over 30) was 10 per cent in 1986, which can be compared to parts of former Soviet Union where obesity was prevalent in 30-40 per cent of the population. In the USA, the corresponding number was 20 per cent, and in Japan and China it was as low as 1-2 per cent. The prevalence of obesity also differs between men and women (in the USA prevalence among women was 25 per cent as compared to 20 for men), between ethnic groups (prevalence among African Americans in the USA was 40 to 50 per cent). There are further whole populations that are obese, according to the body mass index classification, out of which certain islands in the Pacific Ocean and Native Americans are mentioned frequently (WHO MONICA report 1987).

⁴ Body mass index is the most pervasive term used by actors in the medical arena to define obesity. It is calculated through the following formula: body weight/body height multiplied by body height.

Obesity is not evenly distributed in the industrialised part of the world, but is related to class, ethnicity and gender. The white, US American middle class, for instance, is generally less overweight than the African American and Spanish-speaking population in poorer areas. African American girls and women also, according to medical researcher Lovejoy, seem to be more at ease with their appearances, body size and weight as compared to Euro American women, even though the former weigh more than the latter (Lovejoy 2001: 240).

In Sweden, where categorizations of the population in racial or ethnic terms are not as frequent, the consensus on what obesity is is similar but more vague. The “typical” obese patient is said to be a woman with low income and low education level (The SBU report). There is a general picture of the social backgrounds of the obese, and strong connections between socioeconomic factors and obesity. These discourses tend to polarise different social groups – be they ethnic, sex or class-related – when it comes to food, exercise and other lifestyle-related patterns of living, something also evident in the medical literature.

Social scientific research on obesity concentrates on cultural, psychological and social aspects of eating, dieting and body weight. More seldom it puts forward the biologically defined mechanisms that affect our desire for food, its effect on weight gain and ability to recognize and satisfy hunger. Medical research on identical twins, for instance, has shown that genetic factors are important, and that they were likely to be similar in body weight whether or not they grew up together (e.g. Bouchard et al. 1990).

From a constructivist perspective, however, studies have shown that what counts or is defined as biological or genetic is historically variable and contingent. On the relationship between what a disease is and how it is experienced, Johannisson shows that diseases indeed are culturally shaped. However, she continues, this does not mean that the diseases are bereaved of their “biological reality”, but that it is dependent on a number of sense making systems of interpretation (Johannisson 1997: 183).

The social sciences’ relative non-interest in medical studies of obesity is mirrored by a mutual disinterest from medical science in more complex analyses of the obesity problem as a whole, including interpretative cultural and social analyses. At the core of this mutual disinterest are partly differing views on epistemological issues. Where medical research is interested in solving a problem defined beforehand, social science, according to Conrad and Schneider (1992), questions the medical model’s definitions and focus on explanations, perceptions, diagnoses and interventions. They suggest that the medical model makes disease and illness into individual problems, whereas disease and illness can remain societal in social scientific analyses.

The question is what we, social scientists, can learn from the many biomedical studies that have been made. They are important in the sense that they give us quantitative data of how widely spread and increasing obesity is, information on which methods have been most successful for weight loss, as well as genetic knowledge on who is at risk of becoming obese. But to understand what data emanating from biomedical research mean in social, economic, organisational and cultural terms, social scientific analysis is needed.

This is especially true when it comes to the medical condition of obesity. A cultural preoccupation with dieting and slenderness is something that, still today, affects women more than men, for example. This explains why body weight and eating disorder became a topic for feminist research at the end of the 1970's (i.e. Orbach 1984, Bruch 1978, Chernin 1985/1994). In her book *Fat Is a Feminist Issue*, for example, Orbach sees obesity as a way for women to protest against the role given to them in society. Another example is Chernin who delivers a psychoanalytic perspective on the relationship between eating and mothering.

The differences attributed to dieting and weight differences between different groups of women probably depends, according to historian Stearns (1997), on the level of participation in the dieting culture defined by the white, middle classes. The dieting culture, he continues, can explain the variations between different groups of the population, but not weight gain seen at an aggregate level. Criticism has been directed at this interpretation from a feminist perspective, claiming that Stearns does not take into account how the ideals of slenderness, shaped as they are from the hegemonic, white, middle class, also affect women who are not part of this class. No women are free from the obsession with slenderness, which is why Orbach asserts that obesity is a feminist issue. Bordo argues that the usual treatment of obesity – dietary and exercise advice, and behavioural therapies – does not get to the underlying reasons and identity confusion of the overweight person. The great effort and work needed in order to guard ones appetite – dieting – often leads to failure and this experience of privation can lead to a compensatory over-consumption instead, which in turn increases the feeling of failure and hopelessness (Bordo 1993: 12). Bruch (1978) warns specifically against behavioural modification therapies which she claims strengthens the feeling of hopelessness of the person with eating problems. Also, there is a notion that the dangers of obesity are exaggerated by media, doctors and insurance companies. Instead, these researchers focus on the problems implied in the constant increases and losses of weight, and the consumption of weight loss drugs. Also, they come with a critique against the goal in obesity treatment to lose weight, rather than an aim towards better health.

The issues of obesity and dieting also put a finger on larger tensions in contemporary society. Bordo localizes the preoccupation of weight in a consumer culture with contradictory demands for a continuing disciplined work ethic combined with the ongoing need for limitless consumption. She sees this as a kind of double bind in culture that is articulated in tensions between what she calls the “performance principle” and “letting go” (Bordo 1993: 201), where extremes of these expressions are anorexia and obesity. The methods to solve this double bind are to give in to consumption or to discipline oneself. The behaviour of the bulimic appears in this context to be very rational. Interestingly, feminist research on body weight has not seen obesity as a medical problem. Instead, it has seen it as a problem related to gender relations and culture. Consequently, the problem of obesity reflects an exaggerated focus on slenderness where efforts to lose weight are part of the subjugation of women.

The medicalisation of obesity

The intense focus on obesity as not only a social or psychological problem, but also a medical one is relatively new. Obesity has become medicalised. Doctors participate in growing national and international obesity research organizations and obesity is increasingly presented as a health risk. What is defined as a disease varies, seen from the longer perspective (Illich 1976, Conrad & Schneider 1992, Conrad 1992). Feminists have traditionally been critical towards medicalisation, since it often has been the “natural” processes of women’s bodies that have become medicalised. This feminist critique has built on a concern that medicalisation is part of a patriarchal process to take away women’s control of their own bodies.

Not only feminists are critical to labelling obesity a disease, however. In 2002, the Swedish Council on Technology Assessment in Health Care published the report “Obesity – problems and measures against it” (SBU report), written by an expert group of medical doctors. This project group defines obesity as a disease, but emphasizes that it can be prevalent “without serious complications or disabling conditions” (Ibid: 8). The Council’s report is an examination of “the scientific foundation for mainly medical measures against obesity” (Ibid: 10) and consists of a reading of international medical scientific literature in the area. The Council’s task was to critically evaluate the scientific basis for medical innovations, existing routines and practices within the health care sector. Among the doctors working with obesity there was consensus around defining obesity as a disease. The board of the Swedish Council on Technology Assessment in Health Care, however, resisted the use of the term disease and chose instead to see obesity as a risk factor. According to the project leader for

the report the debate became polarised, since the state recently had taken away subsidies on two drugs that were seen as a major part in elevating government expenditure on drugs, namely the weight loss pill Xenical and the potency drug Viagra (telephone communication, 17 March, 2003). In the debate, representatives of the public sector, such as the county administration board, *Landstingsförbundet*, ended up taking the view that obesity was seen as a risk factor such as high blood pressure or smoking.

Reports such as this one play a certain role in decision making processes involving health related issues. The report can be seen as an example of how medical research becomes established as facts in contexts outside of medicine, and how medical research comes to define problems that in the long terms also affects the practices of obesity treatment.

The medicalisation of what was perceived of as cultural or social problems was taken up within medical sociology from the 1970's (Illich 1976). Illich did this as a way to politicise notions of health and illness, and show how social and political problems were hidden under the umbrella of medicine. Conrad and Schneider also conduct research into how structural circumstances, such as socio-cultural, environmental and material questions, are made more or less invisible in a medical model (Conrad and Schneider 1992). According to Conrad, medicalisation consists of defining a problem in medical terms, using medical terms to describe the problem, or using medical interventions to solve the problem. Medicalisation occurs when a medical frame or definition is used to understand or deal with a problem, be it alcoholism, homosexuality or obesity, behaviours that earlier have been seen as immoral, sinful or even criminal, but not necessarily medical. In the "westernised" world, medicalisation of human problems has foremost occurred when it comes to deviances and natural life processes such as drug use, mental conditions, eating disturbances, sexual differences and learning problems. More recently, the term "risk" has come to substitute older ideas about reasons for unwanted conditions (Lupton 1991: 46).

The high costs for drug consumption have engendered debates about which health problems should be classified as disease and which should not. Here, some actors want to make a distinction between disease and risky lifestyles. This type of argument makes it easier to separate diseases whose drugs are to be state subsidized, and states of risks whose drugs are not to be subsidized and instead taken care of by the individual. Persons defending the subsidy for obesity drugs, e.g. obesity researchers/doctors and their patients are often of the opinion that obesity is a disease like any other and that people with obesity are discriminated against enough as it is without condescendingly claiming that it is not a disease they are suffering from, just a bad choice of lifestyle. They ask what the difference is between obesity

and other diseases whose drugs are subsidized, such as diabetes and asthma. They point out that those patient categories afflicted by risky behaviour, as well. Some go so far as to claim that almost any disease is a result of lifestyle choices.

Obesity researchers and many health care workers active in obesity related care talk of obesity as a disease, whereas government officials see it rather as a health risk or public health problem. Government organisations are not as keen on the category disease, mainly due to the economic consequences such a classification would have for the health care budget. A disease requires treatment. The process behind having obesity classified as a disease rather than a state of risk or public health issue has been successful within many parts of the medical arena, although not all medical professionals agree to the classification. Sociologist Anna Johansson (1999) has shown that the disease definition gives interpretative priority to medicine and that overweight persons are not helped by being classified as sick. Moreover, this classification makes it possible for doctors to further moralise about patients' lifestyles.

There are different explanations of what the causes of medicalisation are. Some argue that medicalisation is part of wider societal processes of industrialization and bureaucratization (i.e. Illich 1976) Still others argue that medicalisation is a result of the medical profession defining what constitutes health and illness, respectively, as a way to extend its professional dominance (i.e. Freidson 1970). Others have pointed out that medicalisation serves particular interests of different institutions and actors. Medicalisation has been seen as being in the interest of institutions responsible for controlling deviance; prisons, schools and the family. Medicalisation has also been shown to serve the interests of, or in fact be pushed forward by the pharmaceutical industry (i.e. Doyal 1979). It has also been claimed that new genetic research on obesity will also affect the degree of its medicalisation (Sobal 1995).

Obesity is an interesting example of medicalisation, but from what has been said above, we can conclude that obesity is only partly medicalised. On the one hand the health care system (in a wide sense including research and development of drugs) increasingly has focussed on overweight and obesity. Medical research and the knowledge produced is being spread outside of the medical community, which means obesity is becoming conceptualised in medical terms even outside of the hospitals and general practitioners' offices. An example of this can be seen in the way many weekly magazines, mostly directed towards women, help their readers to find their body mass index, to indicate where they are on the obesity scale, and deliver new, miraculous diets.

As I have shown, there are many views on whether or not obesity is a disease and, if it is a problem, how to deal with it. Coming up with a description of what obesity is cannot be done without specifying whose definitions are taken into account, as well as which elements or actors are seen as being part of enacting obesity in a specific situation. Such a perspective is in line with a constructivist stance which implies that obesity is not something “out there for all to see”, but rather something that is enacted in practices that are temporally and spatially situated. The biological reality is enacted differently by groups of obesity researchers, dieticians working with obesity, governmental organizations or organizations for the overweight/obese.

Li mi tations, purpose and research questions

I motivated my choice to investigate a clinical trial of an obesity pill in two broad ways. One stems from an interest in what I saw as a continual process of (bio)medicalisation in society, with obesity as an example similar to other, newer, so called lifestyle diseases such as back aches and impotence (i.e. Conrad 1992, Clarke et al 2000). Secondly, I have an interest in the increasing complexity of clinical trials and more specifically in their characteristics as a significant part of an industrial process of production located in the clinic. Here, changes in the organisation of health care and an increasingly information technology intense and dependent research system are important to investigate (Berg and Mol 1998). Through studying a clinical drug trial I show how different rationalities of health care and industry are articulated by the different people working with the trials. I also analyse different kinds of knowledge being produced around the trial, as well as the co-operations involved in carrying out a trial. Moreover, I look for what may be termed local/global systems of meaning around obesity and clinical drug trials. In this chapter, I have given a background to the following, more specific questions.

However, before these questions are presented, something needs to be said about the dissertation’s limitations. As I have said in this chapter, obesity is a contested area and is perceived of differently by different groups and individuals. Therefore, it is important to point out that this dissertation deals with obesity as represented by the individuals that participate in the trial, and does not include overweight people outside of the medical arena who do not seek medical attention for their condition. The thesis only deals with obesity as represented by those within the medical arena who do consider it a problem, be it one of disease, health risk,

self-esteem, individual psychology or body aesthetics. Furthermore, the thesis does not make claims as to how the trial participants themselves view their condition. It is limited to how obesity is enacted by clinical trial staff.

This thesis is a case study of how multi-centre clinical trial work is conducted and managed in one locale in order to produce data in a way as efficiently as possible, and what happens when the rationalizing tools – a clinical research protocol and a computer control system – are used in practice. The work that is in focus is the more and less invisible work performed by nurses, dieticians and doctors, among whom I have conducted fieldwork. Fieldwork, including observations and interviews are methods employed in order to understand how the work tasks actually are performed in practice and to understand how they themselves viewed their work and the tools they used. They are also methods used in order to investigate how obesity was enacted in the trial. There is, to my knowledge, only one study of a clinical drug trial where this kind of fieldwork has been the main method (Löwy 1996). The empirical focus of my dissertation is unique in that it studies a privately sponsored, large scale and multi-centre drug trial, a field which is difficult to get access to, due to business confidentiality issues. It is also different from previous studies in that the trial involved individual participants who were not patients in the clinic, but enrolled through advertisements. Finally, the focus differs from previous research in that it takes the work of clinical trial staff as its point of departure, that is, it primarily delivers the perspectives from those who perform the everyday clinical work. The focus on invisible work and rationalizing tools makes it possible to discuss issues around the control private firms have over the work performed in clinical drug trials, as well as how staff localize the tools in order to make them work.

The dissertation's main purpose is to understand the complex system of standardized and non-standardized tools and practices involved in large scale clinical trial work, from the recruitment of the participants, the follow-through of the clinical research protocol, and up to the point where the data produced is sent off to the pharmaceutical firm. Three specific questions are asked:

Through what tools and work practices are large scale clinical trials made efficient?

How is the relationship between the rational/technical tools and the experiential/contingent aspects of clinical trial work articulated in a clinical trial?

How is the condition of obesity enacted within these practices?

This chapter has given a background to the main themes of my study. I briefly introduced what a randomized controlled trial is and that it can be seen as an icon of evidence based medicine. The chapter also introduced the study's main concerns, the science/care dilemma and the way industry participates in its construction. It also introduced research that has focused on the technoscientific nature of medical work, something that is needed in order to understand why the focus on the tools involved in clinical trials is important for understanding clinical trial work practice. Finally, it introduced what obesity is seen to be from a number of different perspectives; those of medical researchers, feminist social scientists and state actors.

The conditions under which the pharmaceutical industry operates are complex and need further introduction. Therefore, in chapter two, I describe some developments within the pharmaceutical industry and its involvement in producing obesity pills, explaining why research on obesity drugs is of such importance for competition within the industry. I present two different descriptions of the pharmaceutical production process: a linear and a non-linear view. I argue that the non-linear view is needed to better understand the way in which the pharmaceutical industry operates when it comes to newly medicalised conditions such as obesity. The chapter also presents central actors in the obesity research arena and considers the role of the pharmaceutical industry taken together with obesity researchers, in the medicalisation of the condition.

The theoretical background used in this thesis to grasp the tools and practices involved in clinical trial work are presented in chapter three. Here, the main theoretical concepts "localization" (Berg 1997), "articulation work" (i.e. Star 1991b, Hampson & Junor 2005), "production tasks" (Fujimura 1987) and "enactment" (Mol 2002) are introduced. The empirical data that makes up this thesis consists of a combination of interviews and more or less easily accessible written materials. How I went about collecting this data and why it turned out the way it did is discussed in the methods chapter, chapter four. In this chapter, a picture is also given of the analytical process that led to this text.

Chapters five through ten constitute the main empirical body of my work. In chapter five I turn to the thesis case study itself: the Obe trials which were conducted on a large scale in a number of different locations. I give a description of how a clinical trial is done through presenting details about the Obe trials, introducing the actors and the organization of work involved in different domains of research and health care.

One way for pharmaceutical companies to compete is to make the clinical trial process less costly through increased efficiency. I will show how this is done by a rationalization of the work involved in clinical trials. A short time before the Obe trials were started up, a spin off firm was formed that built on skills developed from computer scientists' work with previous large scale research projects at the clinic. Chapter six describes the activities of this firm, in particular its involvement in recruiting participants to the part of the Obe trials that was a nation-wide Swedish trial.

Another tool to make clinical trial work efficient is the clinical research protocol. It standardizes the different production tasks to be done at the different trial sites. In chapter seven, this tool is described and analysed as a standard without which the trial could not be performed. This standard can be said to represent the trial in an ideal-typical way. In practice, however, the staff using it need to adjust it to fit their everyday practices and the needs of the participants, and to make it work at all. They "localize" it to fit into practice. Chapter eight and chapter nine therefore focus on how these tools are localized in the practices of the Obe trials, and do so in two different ways. In chapter eight, the trial is primarily analysed as an industrial production of data. The chapter focuses the work done by nurses, dieticians and doctors who are the ones working with the trial on a day-to-day basis. A distinction between two types of work is done: routine and standardized production tasks on the one hand and the articulation work needed to align these tasks and make them doable, on the other. It deals with the kind of articulation work Hampson and Junor (2005) refer to as classical management work.

A common problem in performing clinical trials is that participants tend to drop out. In chapter nine, I show that a lot of work is needed to enable the follow through of the protocol, work that is not specified in the protocol itself. I refer to these different tasks done to localize the tools as compliance work. Chapter ten, finally, considers how the condition obesity is enacted in the clinical trial setting and shows that different obesities are incorporated in the protocol due to the coordination of beliefs and goals performed by staff in localizing the protocol. The main points of the thesis are then summarized in chapter eleven, and the implications of the findings in terms of blurred boundaries between research and care are

brought up. It ends with a discussion about what can be said about the medicalisation of obesity from the data that has been analysed.

The pharmaceutical production process and obesity pills

The number of new pharmaceutical drugs available on the Swedish market has increased during the last decades. During the decades 1967-1977 and 1977-1987 the number of newly introduced substances was around 150 whereas in the following decade, 1987-1997, the number more than doubled. The increase in production from year 2000 to 2001 was as much as 21 per cent, the greatest among goods produced in Sweden. Developing costs for pharmaceuticals have also increased and average around 500 million Euro, per registered drug. Out of these, two thirds of the sum consists of costs for products that never reach the market. Only three out of ten pharmaceutical products generate incomes that exceed development costs. Such a scenario has led the industry to work for both a more efficient global marketing organisation as well as rationalizing the development chain through new technology, outsourcing specific tasks to contract research organizations (CRO's) and more efficient process steering (SOU 2000:86:221-24). These increasing costs are a problem both for the industry and the state. Increasing government expenditure on pharmaceuticals through state subsidies is a problem for all OECD countries, albeit to varying degrees. The pharmaceutical industry sees problems in that the R&D phase is increasingly regulated, which makes it expensive to produce drugs.

In comparison to other large industries, the pharmaceutical industry is unique in at least three ways. Its production and marketing of drugs is more regulated than in many other industries. Pharmaceutical production processes are also much more research intensive than other industries. In addition, prescription drugs are, to a large extent, consumed by the publicly financed health care system and through subsidies. This makes the relationship between producer and consumer a special one, where doctors act as both consumers (in the sense that they often are the ones deciding on what drugs to prescribe) and intermediaries between patient-consumers and the pharmaceutical industry.

This chapter provides a background on the pharmaceutical production process by describing a linear view of what the process looks like (cf. Bergenheim 2000, Lemne 1991/1997, Jadad 1998). It then goes on to describe a non-linear view (cf. Fishman 2004).

The non-linear view is needed to understand better the way in which the pharmaceutical industry operates when it comes to newly medicalised conditions such as obesity. The non-linear view is also relevant as part of an explanation of why costs for drug production have increased. The chapter ends with a discussion of how the state and industry, respectively, try to solve the problems involved in increasing costs. The background on how costs are increasing is important in order to understand the ways in which pharmaceutical firms' are trying to make the clinical trial phase of pharmaceutical R&D more efficient.

Producing pharmaceuticals: the standard view

Producing pharmaceutical drugs is a costly and lengthy process that involves the work of many professional groups. It can take up to fifteen years for a substance to reach the market. Finding new substances in the pre-clinical phase is a process where thousands of substances are screened and discarded along the way. The substances are screened and tested both in vivo and ex vivo, that is in cell cultures and, later, in living animals. In the tests, the toxicity of the substance is evaluated, as are its biological effects on the cell or animal body. After months of excess dosage of a specific molecule, the test animals' organs are anatomically and pathologically examined. During the whole process, changes in weight, blood, urine, etc are registered. Tests on pregnant animals also have to be performed.

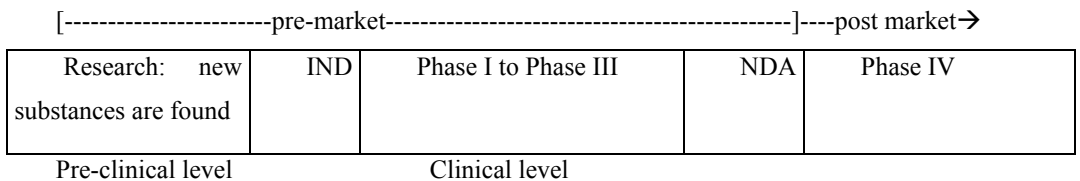


Figure 2:1 Stages in the R&D process (Bergenheim 2000: 16).

When a substance has successfully passed through thorough pre-clinical testing, an application is filed to conduct further tests on human subjects. This “investigational new drug” (IND in Figure 2:1) is then taken further to the clinical level. Clinical studies are

divided into four different phases. In the first phase (phase I), the substance is tested on a small group of healthy volunteers (except when it comes to obviously dangerous substances such as cytostatic agents used in cancer treatment). The goal of this stage is to examine how the substance is taken up, distributed and broken down in the body, and to register eventual side effects, such as headaches or allergies that have not been possible to see in animal bodies.

In phase II, the drug is tested on a small group of patients with the symptoms typical for the disease in question. The goal here is to find the suitable dose of the drug, to see that the substance “works” and to decide whether the side effects are small enough so they do not outweigh the drug’s benefits. Tolerability, safety and efficacy are studied as well as the relation between dosage and effect. Phase II studies have tended to increase in scale, and now often include about 500 patients (Hacksell & Johnsson 1997: 2565).

When the results from phase I and phase II trials are analysed as satisfactory, the drug is tried in a phase III trial, such as the one studied here. This is a large scale study on a sizable group of patients. Phase III trials are mainly used for evaluation of effect and adverse events, especially in relation to already established forms of treatments. They are also used to establish the appropriate dosage. Phase III trials also include evaluations of new “indications”⁵ for an already existing drug. The drug being tested in the Obe trials, to be discussed here, is one example of a drug where a side effect has been turned into a main effect.

When a phase III trial is completed, the data is analysed and summarised and sent to the Swedish Medical Products Agency, the Swedish equivalent of US American FDA, which then decides whether the substance is acceptable for sale to the public. As no pharmaceuticals are free from side effects, the Medical Products Agency performs a risk analysis where the substance has to be shown to have more positive effects than negative ones in order to be accepted. After the substance has been accepted, a large and long term follow-up study of the substance is often performed. This is called a phase IV trial.

Normally, there is a time limit of seventeen years from the point where a firm receives a patent for a new substance to when it delivers the tested and approved drug and makes a profit from it. After that, patent protection runs out. Thereafter, it is possible for other companies to produce their own, often cheaper, generic copies of the drug, and profits are likely to decline. To produce a drug for the market can take up to fifteen years, so sales during the remaining

⁵ In clinical trial discourse an indication is that which is defined as the condition the drug is aimed to treat. It is a more specific term than “condition”, since an indication is related to its (pharmaceutical) treatment. The indication for the Swedish part of the obe trials, for example, is a body mass index over 30 or body mass index above 27 with concomitant risks.

few years have to be substantial to cover the high expenses of pre-clinical and clinical trials, approval processes and marketing of the drug in order to end up with a profit at the end of the day. Every extra month that the drug is on the market and still protected by the patent can mean significant incomes for the companies. Therefore, it is important for the pharmaceutical companies to keep the production time as short as possible. The university based knowledge firm studied in this thesis has found ways to shorten the time needed in clinical trials, which I will return to in chapter six.

This is the linear description of the pharmaceutical research and development process in which a substance is tested and eventually becomes a registered pharmaceutical drug. It is a description that can be found in most overviews of the clinical trial process (i.e. Jadad 1998, Lemne 1991/1997, Bergenheim 2000) and serves as a good way to introduce the formal phases of the pharmaceutical production process.

Producing pharmaceuticals: a non-linear view

The standard linear description of the drug production process has its advantages in that it presents a complex drug development process in a relatively simple way. It describes all the formal steps needed in order to eventually be approved by for example the Swedish Medical Products Agency. In coming to grips with the complexity of pharmaceutical production, the standard view obscures two important issues, however. First, it makes it seem as if every registered drug involves substances that have gone through all the steps in the up to fifteen year long R&D process. It presents a picture where a problem or disease is defined and then substances are looked for and screened to find a new drug to alleviate disease. The more common scenario, however, is that firms look for new conditions to treat with an already existing drug that they have a patent for with another indication: they have the drugs but try to find new conditions to use them on. The scenario where completely new substances are tried for existing diseases is less common. In competing with other companies, the industry is not only looking for new substances but also for new conditions to treat. In this sense the pharmaceutical industry works like other industries; innovations are not driven by needs defined beforehand, as it is often assumed. Rather, innovations are the result of existing technologies combined in a new way or for new purposes (cf Pfaffenberger 1992).

A second problem with the linear view is that it makes it seem as if the marketing of a drug only starts after the drug has been registered. Drawing a line between research and development, on the one hand, and marketing, on the other, is difficult. Marketing occurs

parallel to the R&D process, and is in fact increasingly done prior to the acceptance of a drug by the Medical Products Agency. This is something referred to as “market-orientation” in pharmaceutical R&D and is increasingly relied upon. Pharmaceutical entrepreneurs, according to Gassman, even see market-orientation as the foremost marketing task in the future (Gassman et al. 2004: 79).

Such market-orientation is done in at least three ways. Clinical studies can be seen as related to marketing in the sense that study participants/future consumers are made aware of the product’s existence and benefits (Ibid.: 83). Having been involved in clinical trials, doctors will be more likely to prescribe the drug and study participants will be more likely to demand it. Large scale and long term phase IV trials are often seen as marketing studies. From a marketing perspective, then, clinical trials serve to “cultivate a loyal clientele” within the medical professions (Oudshoorn 1994: 108) as well as with study participants.

Second, pharmaceutical firms’ ways of marketing newly medicalised conditions have become more and more sophisticated. Fishman (2004) shows how the recent medicalisation of female sexual desire, the medical condition called female sexual dysfunction (FSD) is being promoted in Continuous Medical Education (CME) conferences sponsored by the industry. Here, medical researchers serve as mediators between the pharmaceutical industry and its consumers. They are promoted as medical experts while simultaneously defining and configuring a consumer market for the condition. Fishman’s work shows how experts in the USA with celebrity status help promote new conditions through self-promotion by, for example, appearing on talk shows and in popular media giving expert advice. Such education of doctors about conditions is thus part of the marketing of the disease and drug.

Third, medical scientific articles are also an important aspect of the marketing of pharmaceuticals. Scientific articles that mention a specific product in favourable terms play an important part in the marketing of drugs (Healy 2004). This is also done through medical ghost-writing by medical writers in the pharmaceutical industry who write up the scientific articles, including results, needed to market a certain drug. They then search for the scientist to put his or her name on the piece.

These three aspects of market-orientation makes it difficult to separate “clinical” and “marketing” phases of the process of coming up with new drugs. With such a perspective, an analysis of clinical trial work must focus on the ways clinical trial work is part of marketing the condition, as well as clinically providing care for trial participants.

Marketing of obesity drugs

The amount of drugs being prescribed has increased, at least partly, as a result of the market orientation in clinical trials and because of increasing marketing budgets in general. Prescription practices are increasingly affected by this heavy marketing of drugs. What a doctor prescribes is related to the doctor's knowledge and preference for specific pharmaceuticals. It is a well-known problem that it is difficult to get non-biased information about a drug since most information about it is provided by the pharmaceutical companies that produce and sell it. Even in the cases where there is non-biased information supplied, as by the Medical Products Agency, the prescribing doctors do not always follow the advice. This can be seen through the fact that Losec, which is one of the most frequently sold substances in Sweden, is still increasing its sales numbers even though committees have recommended other, similar substances (SOU 2000:86: 71). The marketing strategies for the former have been more successful than the information supplied by publicly funded health care information.

Addressing this situation is difficult. According to a report from The National Board on Health and Welfare, *Socialstyrelsen*, the high prescription frequency of certain drugs over others is due to factors "outside" scientific and evidence based knowledge, or what in the report is deemed as "factors of seemingly irrational character" (Socialstyrelsen 2000: 38). By irrationality, the report alludes to the relation between prescribing doctors and the patient, their "attitudes and values", and "surrounding social factors" such as the marketing done by pharmaceutical companies. Such factors, according to the report, are not possible to include when analysing increases because "many judgements and decisions depend on what happens in the specific prescribing situation" (Ibid).

To confound the situation even more, many drugs receive free advertisement due to the intense debates in media. This has been especially true for the obesity and impotence drugs Xenical and Viagra that relate to topics often addressed in the tabloid press. Through this kind of indirect advertising, patients receive information about available drugs, which can place doctors in a position where they have to weigh the individual patients' wishes and benefits against general recommendations.

Different actors with different views

As medical knowledge increases about the risks of obesity, so does the need to help those obese people seeking help. However, health care resources are scarce and obesity is a low priority area within the public health care sector. Those seeking help are often enrolled in different obesity related research projects. A considerable number, but far from all, of these projects involve pharmaceutical research. Since I started my research, several investigational drugs have been tested on a large number of participants.

In Sweden, a small amount of people, around 90 individuals per year, are given the possibility of obesity surgery. This is the only existing effective clinical weight loss treatment, even though it is costly and can lead to serious and irreversible side effects. Other methods, such as dietary and exercise advice or drug therapy, have been shown to be effective only on a short term basis. Two years after such treatments, most patients have regained the weight they lost. The two existing pharmacotherapies, Xenical and Reductil, are both costly and ineffective (Hedqvist & Eggertsen 2002), and studies have shown that the weight lost through successful interventions is in the majority of cases, regained when the intervention ends (Maggio 1997).

Between 2001, when I started doing this research, until 2005 when the dissertation was completed, there were two obesity drugs on the Swedish market: Xenical and Reductil. Xenical has been available on the Swedish market since February 1999 and was on the top ten list of prescription drugs up until April 2001. Xenical is a lipase inhibitor for obesity management that works in the intestines, where it inhibits the absorption of dietary fats. At the recommended dose it inhibits fat absorption with approximately 30 per cent. Patients are told to use Xenical in combination with a diet regime and a vitamin supplement. Potential side effects (more likely if the diet regime is not kept) include “gas with discharge”, “increased number and/or inability to control bowel movements” (Medical Products Agency 1998).

The second obesity drug available on the Swedish market, Reductil is a substance belonging to the family of Selective Serotonin Reuptake Inhibitors (SSRI). It lessens hunger feelings and the amount of weight loss is similar to that of Xenical. Potential side effects of using Reductil, are increased blood pressure and heart beat frequency. Reductil became a registered drug in Sweden in April 2001, the same month governmental subsidies for obesity drugs were withdrawn. Since then, patients given a prescription for both drugs have to pay for it out of their own pocket, except in the most severe cases where the prescribing doctor can apply for exemption on behalf of the patient.

The process of receiving approval for a drug means that the appropriate “labelling” has to be done, i.e. the effect of the drug has to be matched with the indication the drug is to alleviate. For example, the formal criteria for prescribing Xenical is that the patient has a BMI of at least 30 kg/m² or a BMI over 28 kg/m² in combination with coexisting risk factors. The treatment is only supposed to be given if the patient succeeds, through his or her own efforts, to lose a minimum of 2,5 kilos during a four week period. If the patient has not been able to lose at least five per cent of the body weight, calibrated at the beginning of the treatment, the treatment should be terminated (Medical Products Agency 1998).

But, the recommendations as to how to prescribe a drug are just that – recommendations. How the individual general practitioner follows them varies. It can be postulated that the recommendations were not followed, since the result of the Xenical launch in Sweden was a large frequency of over-prescription. When Xenical came on the market in February 1999, it immediately rose to the top ten list of expensive drugs (Socialstyrelsen 2000: 27). Its popularity is remarkable considering the fact that the substance has very small effects in general and that only a small proportion of the obese respond to the treatment with “clinically relevant weight loss” (Medical Products Agency 1998).

The marketing of Xenical was quite successful; both through the campaigns aimed at general practitioners and other prescribing doctors, and, less evidently, through the intense tabloid media coverage of both of these new and miraculous obesity drugs. There were also “information campaigns” that focused on overweight and dieting more generally. Compared to other disease areas, obesity issues have an advantage when it comes to marketing of new drugs, since body weight, dieting and slenderness are issues that generally preoccupy many people’s minds.

Considering the low efficiency of all existing medical treatments for obesity, aside from surgery, how do those who are thought to need them reason around different treatments? I interviewed a spokesperson from the Swedish organisation for overweight and obesity, *Överviktigas riksförbund*, an organisation with around 260 members in the year 2003, which works with everyday problems like finding clothes in big sizes, and also lobbies for more health care resources. The organization has not come to a consensus on whether obesity is to be seen as a disease or a risk, and has instead wanted obesity classified as a disability, which would mean obese people could receive the same kind of social benefits as other disabled people (i.e. mobility services). The opinions concerning different treatments differ between individuals within the organization and the organisation does not have a united stance in the sensitive questions (Interview 22/10 2001). For example, there are some with severe side

effects from obesity surgery and others without and who therefore think it is the best thing they ever did.

The spokesperson for *Överviktigas riksförbund* said he personally fears that obese people are treated more and more like guinea pigs. Research is needed but so are treatments. There is very little available apart from that related to the research and testing of drugs. But drugs involve a risk of becoming addicted to them, since stopping a medical treatment is known to cause weight gain. This, taken together with their at times unpleasant side-effects, means that research on new drugs for obesity may not be an answer to the problem, at least according to *Överviktigas riksförbund*. The spokesperson I interviewed said that only 90 persons in Sweden were being treated for obesity at the time. The rest were involved in research-oriented treatments, mostly clinical trials. But in his view, the only way to lose weight is through eating less, exercising more, in addition to strong, individually adjusted, psychological support.

The National Association to Advance Fat Acceptance (NAAFA) in the USA is more critical in its views on dieting and the pharmaceutical industry. Their basic standpoint is that overweight people's physical and psychological well-being should be considered before strict weight loss regimes, including drugs. NAAFA also asserts that a disease classification makes it possible for doctors to moralize over patients' lifestyles, and is also critical towards obesity research's focus on obesity as a health problem, and stresses the need for researchers to consider obesity as a psychological, cultural and political question. The development of the idea that obesity is a disease that should be treated, that is the medicalisation of obesity, is seen to be strongly connected to certain actors' economic interests. NAAFA therefore lobbies for the National Institute of Health (NIH) to break off its funding of dietary and pharmaceutical treatments as well as of obesity surgery (see www.naafa.org). *Överviktigas riksförbund*, in comparison to NAAFA, appears to trust and agree with the medical profession in how it formulates the problem of obesity, even if the issue of obesity drugs contains some controversy among its intended consumers.

The effects of increasing drug costs

One of the main problems for the pharmaceutical industry is that most drugs on the market do not sell enough to make up for their costs of R&D. To analysts of drug development it is well known that it is not possible for pharmaceutical companies to produce drugs for so called diseases of poverty in less developed countries, due to lack of a market that has the ability to pay. What is less well known is that it is also not economic to produce drugs for major illnesses in more developed countries, unless they are sold off-licence for other indications, or sold off-licence over the Internet. In order for the industry to stay alive, it has to find and develop so called blockbuster drugs (drugs earning more than 1.5 billion dollars per year). “Lifestyle drugs” are those that can deliver this kind of economic gain for the industry. These blockbuster drugs, if they end up on the list of subsidized drugs imply that already strained health care systems and governments spend larger and larger parts of their budgets on pharmaceuticals. Considering the increasingly intense and sophisticated ways in which pharmaceuticals are being marketed, it is not surprising that the costs of governmental expenditures on pharmaceuticals have increased greatly.

Increasing governmental costs cannot only be attributed to new drugs and recently medicalised problems such as obesity and impotence, however. The general consumption of drugs in Sweden is increasing, although not to the same extent as e.g. in the USA, even for diagnoses that have been around for a much longer time (SOU 2000:86: 86). More new drugs are being introduced than before (Ekelund 2001). Half of the drugs on the market today did not exist a decade ago (SOU 2000:86: 11). This general increase is partly due to demographic changes, such as the growth of an older population which consumes more drugs than a younger population. The general increase in consumption is also related to the prescription situation itself which contributes to increasing consumption, and hence costs, of drugs. According to another report, financed by the County administration board in Sweden the most important explanation can be found among the prescribing doctors. The specific knowledge and incitements of the prescribing doctors, they conclude, are central when looking into the reasons as to why costs go up.

An additional explanation for increasing pharmaceutical costs, albeit in a Canadian context, has been attributed to the lack of time and high work pressure in the public health care system, which in turn relates to decreases in funding for the public health sector (Lexchin 1999). This lack of time and resources would mean that doctors prescribe pills for the patient, rather than other, more time-consuming, treatments.

It is difficult to say which of these explanations are most significant in order to explain the increasing costs pharmaceuticals are placing on the national health care budget. Different actors can be assumed to state different reasons, varying according to their different perspectives. For example, pharmaceutical companies tend to put the blame for increasing costs on the increasing bureaucracy involved in the research and development stages of production while government officials stress other reasons, such as companies' increasing expenditures for marketing.

The high costs of producing drugs are a problem both to the pharmaceutical industry and the state. Pharmaceutical costs have increased to such an extent that the state has had to take measures to keep the costs down. One way for the state to keep costs down is to limit the number of "newer" conditions in the subsidy system, *Läkemedelsförmånen*, as was done in Sweden in April 2001 when obesity and impotence drugs were withdrawn from the list. The paradox in the case of existing Obesity drugs is that the successful marketing has made them too popular and it is popularity that has meant an end to state subsidies. Had the marketing been less intense and the desires to lose weight less widespread, then perhaps the drugs would have stayed on the state's list of subsidized substances. This example also shows that excessive marketing may become counter-productive in a system where most health care is paid through state subsidies. If a drug becomes too popular, but not seen as efficient enough, the state will decide that it is not worth paying subsidies for it.

The pharmaceutical industry has developed several different ways to cope with the high costs involved in developing new drugs. One way is to shorten the development process and make it more efficient. A shorter development process means a longer time for the drug to be on the market before the patent expires. Even though industrialists and clinical trial research doctors complain over increasing work loads due to increased regulatory requirements and more complex research processes, Abraham and Reed (2003) argue that the research process has actually become quicker. New firms, such as the one described in chapter six, are established, with the primary purpose of making the trial processes more efficient. These firms conduct specific, outsourced tasks, handle laboratory tests, recruit trial participants and manage the development processes locally. By outsourcing these tasks, companies hope to rationalize the production process and make it more cost efficient.

There are different ways in which the pharmaceutical industry tries to cut costs. With a non-linear understanding of the R&D process, the practices that make up what "marketing" and "research and development" are, respectively, cease to be self-evident. This chapter has brought up marketing strategies, including "educating" the market about what diseases they

may have and can get relief from. Such market-orientation in pharmaceutical R&D is only one way to make the development process more efficient. Other, more traditional ways to do this include computerization, commercialization and standardization of different work tasks.

Conceptual framework

The focus of this study is the work performed in localizing rationalizing tools involved in one large-scale, randomized controlled trial, an important phase in the production of pharmaceuticals. An overview of some of the more general perspectives and issues in forming this study, the technoscientific nature of clinical practice, the role of industry in clinical research and the science care dilemma, has been given in the introductory chapter. The rest of this study will look at the work being done in an RCT. What does it involve? In what ways can it be made efficient without lowering the participants' or staff's willingness to participate? And, how is, simultaneously, the condition being investigated, obesity, enacted by the different actors involved? I have found Berg's concept of localization, Fujimura's distinction between articulation work and production tasks, Hampson and Junor's conceptualisations of articulation work and Mol and Law's use of the term enactment useful to explore these questions.

Concepts used by the actors in the trials discussed here are loaded with different kinds of meaning, as are the concepts used by social scientists to describe diverse kinds of medical work. During the research process leading up to this text, many such theoretical concepts have come and gone, before I settled on the ones presented in this chapter. Recurring terms that were used by informants, (i.e. "sponsor" and "compliance") have meant more than I could imagine at the beginning of analysis. Concepts from the field of science and technology in society, STS, have also helped me along the way only to prove untenable at a later stage. To give an accurate description of how the theoretical concepts presented here came to be used is difficult, and will at best seem self-evident looking in the rear-view mirror. Coming up with the "right tools for the job" to analyse clinical trial work, to cite Clarke and Fujimura (1992), has been arduous analytic work.

Not only human actors are in focus in this study of a clinical trial, but also technoscientific tools. Accentuating the importance of certain tools enables a different understanding of the clinical trial than one would have with an emphasis on the human actors only. In my study, both perspectives are present. Two tools are central to my presentation and analysis: the clinical research protocol and a computer control system. The protocol is a

lengthy document that includes all the information needed for conducting the trial, from the purposes of the study, via the drug's pharmacokinetic profile to information on the exact tests that are to be done in the trial. The computer control system is a tool that manages the trial work on a macro level, and sees to it that all the many and detailed tasks are performed in as smooth a way as possible. Both these tools are used to coordinate and control the clinical trial.

In this chapter, I first present the concept rationalizing tools used by scholars within science and technology studies to describe the protocol and control system and discuss the way work is being standardized with their help. I use the notion of work in the way used by researchers connected to the tradition of symbolic interactionism to depict what is being more or less visibly done in the trial. The process of standardization becomes relevant in order to understand the relationship between the tools and the work. Finally, I draw on constructivist science studies in describing how obesity is enacted in the trials.

Rationalizing tools

Research protocols are used in clinics all over the world and can be seen as sets of instructions to help staff at a clinic know what is to be done at a particular point in time. These instructions can be more or less detailed and elaborate, or read as suggestions and binding, and can have different appearances and structures. They can consist of very general recommendations or can be in the shape of a very precise chart showing exactly what to do in a certain situation. What different protocols have in common is that they guide staff through a sequence of steps. They also function as a focal point of reference to which various members of staff refer and can orient themselves by (Berg 1997: 52).

Rationalizing tools, by Berg variably referred to as coordinating and accumulating tools, are used in medical practice to avoid mistakes in everyday clinical decision-making. Built-in within the tools is expert or scientific knowledge about a specific scenario that is supposed to aid each individual doctor to make a scientifically informed decision, rather than relying on individual clinical judgement. Advocates of such tools stress the work made possible through them. Conducting a large scale research project such as the Obe trials in a standardized way in many different places would not be possible were it not for such knowledge-based tools.

The power of standards is often underestimated in social theory. Standardization is, as Barry states, often taken for granted and seen as a technical matter best left to specialists. Barry argues instead that standards play a critical part in political and economic life (Barry

2001: 205). It has been stated that complex and large-scale projects cannot do without standards (Star & Bowker 1999: 13 ff.). The standards serve an important function in that they make things work in as similar a way as possible across distances. Standards are: 1) efficient instruments for information, 2) a good method for coordination, 3) able to reduce complexity, allowing overview and understanding (Brunsson & Jacobsson 16ff).

Critics of standardized tools focus on the impossibility of capturing local conditions; they are too uniform to fit smoothly into actual, diverse medical practice. Also, there is a concern that the tools make medical personnel into “mindless cooks” who simply follow instructions. Along with this fear also comes a fear of deskilling.

Standardized tools, as Star has pointed out, are problematic in that they do not fit into every practice and with every person they are designed to work for. They can become problematic for those whom they may not have been standardized for (Star 1991a). Also, not all work is standardized. Which work tasks become standardized and which do not depends on power relations in the work place and in society at large.

Berg notes that both critics and advocates “debate the nature of the tool and practice” (Berg 1997: 161). In so doing, both sides reify either the tool or the practice in a “foundationalist” manner, overlooking that the qualities of both are not pre-given, but constructed in relation to each other. To him, there is not a one-directional process of a tool having “effects” on practice; instead medical practice and the tool are co-constructed in specific situations. This means that the degree to which the tool deskills its users or shifts the control of decision-making is not self evident.

A site of practice consists of several different kinds of actors with specific histories, routines and interests, and there are local variations as to how a tool is made to work. They can be very detailed and specific, but they can never fully control what is done in practice. Berg has studied different types of rationalizing tools in the medical situations in which they were used. His argument is that no tool is used exactly in the same way in every single location and he shows how different staff members “localize” the tools to make them work in the particular situations (1997: 152). In Berg’s words, getting a rationalizing tool to work,

...requires leaving [staff] the leeway to digress from the tool's prescribed steps, to skip or skew input, or to sometimes just avoid the tool completely [...] It *requires* allowing medical personnel to adjust the tool to their ongoing work. It requires that the tools become part and parcel of local work routines. It requires, thus, a further *localization* of the tool: a moving away from its ideal-typed universality and uniformity.

(Berg 1997: 152, his italics)

The tool may be said to discipline practice, but practice cannot ever be fully disciplined. In getting a tool to work, the two processes of localization and disciplining occur simultaneously. The point I want to draw out here is that simply following instructions will not make the tool work. In order for this to happen, staff will need to make adjustments as well as find ways to deal with the ad hoc characteristics of everyday work, as I show in chapters eight and nine.

Invisible work, articulation work and production tasks

It is difficult to analyse the meaning and function of tools outside the specific practice where they are used. Tools are often designed to make work tasks more effective, or more rational. Some kinds of work are more often put in the spotlight by employers in an organization, while others often are made invisible (Shapin 1989; Strauss 1985; Star 1991a; Star 1991b). The skilled work of laboratory technicians involved in the production of scientific knowledge is often made invisible, both by the scientists involved and by the social scientists studying them. It is considered to be work that needs to be done, but that “anyone can do [...], that such workers are easily interchangeable on the labour market, and that no knowledge-ability and little skill are involved in its performance” (Shapin 1989: 557). The work of low status groups tends to be neglected which is why Shapin talks of “the invisible technician”. Gender studies have similarly noted that women laboratory workers, or women's involvement in general in science is rarely studied or acknowledged (Smith 1988; Berner 2004; Wajcman 2004). This may be due to a predominant focus on the ‘heroes’ or creators of science and technology and not on persons who use the tools.

The tendency to make relatively low status jobs invisible exists in research on clinical trials as well. The users of the rationalizing tools have largely not been studied. Harry Marks' (1997) work on the history of clinical experiments from 1900 to 1990, for example, focuses on those he terms "therapeutic reformers", and includes persons involved in the design of clinical trials and research protocols. It does not, however, include those whose work it is to use these protocols. Also, in Epstein's book dealing with clinical trials in AIDS research, the work practices themselves are not visible, and neither are the technicians performing them. Oudshoorn's study of clinical research directed at finding a male contraceptive method is an exception in that she mentions the diverse forms of work that nurses perform in order for the participants to stay "compliant" to the protocol (Oudshoorn 2003: 177ff.)

In my study, the work performed by such invisible technicians is visible. The workers in the basement of the clinic involved in the Obe trials are seen as an important part of the knowledge produced, but their work is seldom analysed in studies of clinical research. To capture what they do, concepts originally developed by Strauss et al. will be useful. They have described the work done by low status workers in the context of a hospital, such as articulation work, comfort work and shit work (Star 1991: 503ff.). The concept articulation work is particularly useful for my analysis, especially in contrast to production tasks.

Articulation work describes the pulling together of heterogeneous elements of practice together in a purposeful and successful manner (Strauss et. al. 1985). I use it to describe the work needed to localize the rationalizing tools. In the process of articulation work there exists interpretive flexibility, which means that there is always the possibility for negotiation, and the resistance someone or something offers also creates and reinforces the openness of the process.

In Star's words, the counterpoint to articulation work is routine. By this she means "that which is packaged up, taken for granted, black boxed" (Star 1991b: 275). Fujimura makes a similar distinction between articulation work and production tasks, where the latter is a relatively clearly defined task (1987: 258). Articulation work, on the other hand, involves planning and coordinating the production tasks. The clearly defined routine work is that which becomes visible in the canonical representation of work as depicted in the rationalizing tools. Using this formulation, I will call work represented by the tools "production tasks", whereas the work that goes in to making these production tasks doable I will refer to as "articulation work".

It is important to note, however, that there is no clear-cut boundary between articulation work and production tasks, and the distribution between the two is also subject to change over

time. For example, one large problem in clinical trials is to make sure that participants show up according to schedule. Nurses have to find different ways to motivate them to come back, even sending reminders to participants or telephoning them prior to their scheduled visits – a planning and coordination that can be characterized as articulation work. Once these tasks have become a routine procedure, however, they are incorporated into one of the many instructions specifically specified in the protocol, and hence turned into a production task. In other words, relatively invisible and taken for granted articulation work, such as sending reminders to participants, can be turned into a well defined production task. This transformation of local routine articulation work into a standardized production task can discipline work but, on the other hand, it makes the contingencies of real work invisible. It represents work as “smooth unproblematic sequence of events” (Star 1991b).

Distinguishing between articulation work and production tasks is useful for understanding the relationship between standardization and work. A task that is routine but not visible in the staff-employer relationship can be transformed into a standardized production task and thereby made more visible. Many different kinds of work tasks can be categorized as articulation work, however, and in the literature that make use of the term, varied and sometimes incompatible concepts of articulation work are used. For the purposes of this dissertation I depart from the discussion on how the concept has been used provided by Hampson and Junor (2005: 168ff.). Two different meanings of articulation work will thus be used. The first is one which consists of ‘classical’ management work. This is the kind of visible work that involves tasks such as planning, organising, coordinating and controlling (Ibid: 168). Such work is performed at different levels of an organisation.

The second meaning of articulation work is what Hampson and Junor refer to as invisible. There are different degrees to how easily the invisible articulation work is uncovered. The benefit of a focus on articulation work is that such a framework can register forms of work that are in danger of remaining invisible. Examples of invisible work include work that takes place but is not registered within the employer-employee relation, work that is externalised from the organisation and work that includes tacit skills, for example skills that appear “natural” (as care work often is).

Enacting the body

The focus on tools and practice has consequences for the epistemological and ontological issues of what the trial is about, namely finding a drug against obesity. Which theoretical perspectives can be used to understand how the condition of obesity is constructed within the trials? Within feminist constructivist studies of medicine and the body, several studies have focussed on the constructed nature of knowledge about the body. The physical body is not there for all to see, and is up to science to discover or reveal. Every description of the body is necessarily social. Constructivist science studies have shown how knowledge about the body is situated and reflect and reproduce existing power relations between women and men (Haraway 1991, Martin 1991). For example, Martin showed how medical textbooks' descriptions of the moment of conception reproduced male and female stereotypes. The egg was seen as passive and the sperm as active. Stereotyped conceptions of what were male/female characteristics thus became reproduced in the textbooks despite their lack of scientific foundation. Feminist research has further shown that knowledge of the body has often been built on a male norm (Berner 2004). This has led to intense epistemological discussions around the knowing subject and whose knowledge it is that counts (c.f. Harding 1987).

A more recent line of study goes beyond analysing such representations to looking at how representations, tools and actors together shape what the body is in situated practices. This is the perspective that will be used in this study. What I am interested in is not primarily what the actors in the trial know about obesity from experience or from possibly gender biased medical education, but rather how they “do” obesity in their everyday trial practices. Such a perspective is in line with what Mol sums up as a praxiographic stance where practice becomes the central site of an investigation. In Mol's words, this recent wave of research “[...] no longer follows a gaze that tries to see objects but instead follows objects while they are being enacted in practice” (Mol 2002: 152). These studies, further, imply “a shift from asking how sciences represent to asking how they intervene” (Ibid.). Such a focus on practice and tools, and indeed intervention, rather than on how knowledge is represented, however, makes way for a different line of research that is, arguably, more useful for the medical practitioners themselves. The focus on the construction of knowledge is here replaced by a focus on what is done; what people do is analytically privileged over what they know. For the purposes of this study, it is how obesity is enacted, in a situation involving tools and practice that becomes interesting.

To summarize: understanding the tools and practices that make up clinical trial work I use a number of theoretical tools that all relate to the wider concept of work. A distinction will be made between the routine production tasks and the often, but not always, invisible work that goes in to aligning them in a way that make them doable: articulation work. The difference between these types of work is not rigid, though. Articulation work that becomes routine can become standardized, and thus turned into a (mere) production task. Tools that enable such standardization, rationalization tools, are widely used in medical practice. They vary in shape, scope and content, but they all have in common that they discipline practices to varying extent. The ways in which they are used by staff does not necessarily imply making staff into “mindless cooks” simply following instructions, though. Instead, in order for the tools to be an aid in getting the job done, a significant amount of work is put into localizing the tools to fit into the specific practice.

This localization is performed through different types of articulation work, out of which I will focus on three different kinds in chapters eight, nine and ten, respectively. In chapter eight it is the ‘classical’ managerial work that is in focus which includes coordinating and scheduling the production tasks. Chapter nine focuses on a less visible kind of articulation work, what I sum up as compliance work. It is the work involved in motivating participants to stay in the trial, and be reliable test subjects: tasks that include counselling and encouraging the participants. Finally, chapter ten focuses a more symbolic kind of work in the localization of the tools. It asks the question of how the objects “obesity” and the “obesity pill” are enacted by the personnel in the clinical trial, and it involves the work of coordinating different beliefs of these objects, a work that is needed in making sense of what it is the trial is about.

This conceptual framework leads to an investigation of the local practices and discourses at one specific trial site, where the different kinds of work will be equally interesting as the tools involved in the conduct of the trial: the clinical research protocol and a computer control system. These tools, together with the diverse tasks performed by personnel, not only produce reliable data, but also enact ideas of what obesity, and its treatments are, in the specific situation. To perform this investigation into how clinical trials are conducted I have performed observations and interviews to analyze the kinds of practices and discourses that

surround them. To understand the character, function and role of the rationalizing tools, I additionally have studied various types of documents that describe their technical details.

Investigating clinical trial practices

How one finally carries out a scientific research project is often different from its original design. The design can be very broad and loosely knit, or it can be an attempt to answer one specific and narrow question, the former is more common in social scientific research. In some ways, research is an iterative process: a continuous oscillation between what you have defined as theory and data, and questions and answers, respectively. The process also has the character of being non-linear and intuitive, taking the researcher on a walk along several different paths (Berner 2005). A design often needs to be modified as you go along. My own modifications along the way resulted mainly from two things: difficulty of access to certain areas of the field, and limitations on what could be said from the data that I finally collected.

In this chapter I will discuss how I went about accessing the field of pharmaceutical research and development, and then discuss the somewhat ambiguous role I ended up having within it. The choices I made for data collection, fieldwork consisting of observations, interviews and documentary data, are then introduced and discussed, as is how the data was analysed. The chapter ends with a reflection over aspects of validity and reliability in representing clinical trial work.

Access to the field

As it turned out, it was difficult to gain access to sites of pharmaceutical experimentation, and in particular to its related documents, something that came to shape what was in fact possible to do by way of data collection. As others before me have observed, it is difficult to access information from the pharmaceutical industry (Lexchin 1999) and especially those sites where clinical trials are performed.

In my very first contact with the obesity research world, when trying to get access to one clinic in Sweden, I was asked bluntly: “What’s in it for us?” The professor at a clinic wanted to receive something in return, such as “good publicity”, co-publication with one of their doctoral students or, if this did not occur, economic compensation for the time it would take for his staff to assist me. Research in the medical world, it seemed, was a question of

exchanging favors. This was also evident from the way everyone who has contributed ever so little in a project becomes an author to a published article. Not being familiar with this view of research as a collective exchange endeavour, his frankness baffled me. Since I could not think of an article to write straight away, and could not guarantee good publicity *à priori*; and since paying people to be interviewed is not common practice in the social sciences, I decided to try to access another site of research.

The second hospital I approached was positive and open towards having me investigate their work. Surprisingly, considering my first difficult encounter with the field, there were no problems for me to access this second site, where I ended up conducting fieldwork. My first contact person there was the dietician Disa. When I asked her about the possibilities for me to do observations and interviews in the obesity clinic and department, she recommended that I contact the medical doctor, Magnus. He was formally, though he had little part in the day to day practice of the trial, responsible for the trial that came to be my focus, the Swedish Obe trial. His reaction was also positive, and he became my gate opener, and also my advisor. From my first days in the field, he was very helpful in showing me around and introducing me to everyone we met, both at the research department and in the clinic, and letting me tag along to the meetings he had during that first day. He also helped me to get permission from the pharmaceutical firm, PharmaCo, to use the international and the Swedish Obe trial as a focus for my study, in addition to formal permission from the head of the department to spend time there. The double character of my relationship with Magnus – who was both an informant and a co-supervisor – was perhaps a bit confusing to both of us as my fieldwork progressed and we each learned more about the other's research conditions.

That said, it was very helpful for me to have Magnus as a co-supervisor at the onset of fieldwork. The terms for my study were discussed directly with Magnus' contact person at PharmaCo. I did not have to sign any papers at the onset, and access was agreed upon on an informal basis, based on trust. Furthermore, an application for approval from the ethics committee was not necessary since the study did not directly involve participants or patients in clinical trials. Those who are involved, i.e. mainly nurses, dieticians and doctors, were informed of the purpose of the research in what can be called a non-standardized form of informed consent. At a lunch seminar, attended by around 15 individuals who were mostly research doctors, I presented my research design. With those I met in other situations I also made clear the reasons for my being there. Each individual was moreover, to the fullest extent possible, guaranteed anonymity. In specific cases where anonymity could not be completely guaranteed or where informants wished to inspect my material, I have sent the interview

excerpts for them to look over. In one case, and on the informant's request, I also sent the interview excerpts as they finally appear in this book for one informant to comment on. The interviewees have thus had the possibility to make clarifications to what they said during the interview. One took the opportunity to do so, and we agreed on how the final text would be formulated to be able to accommodate the particular interviewee's concerns. These ethical concerns, which follow the basic principles set out by the Swedish Research Council of Humanities and Social Sciences guidelines for ethical research, were important for me in the research process, especially when I wanted to establish trust and thereby access to the field.

An ambiguous role in a fluid field

According to anthropologist Helen Schwartzman (1993: 48), it is in the first contacts with the field that the greatest differences are seen between the researcher's and the informants' culture. In my case it was the initial problems of getting access that signalled what the differences were between being a researcher in a social sciences department and one in a medical science environment. This insight led to many informal conversations with researchers at the second hospital, comparing research funding, terms for doing a PhD and the differences between qualitative and quantitative research methods. Of greatest relevance to the dissertation's focus are the differences in how our respective research is funded and financed, i.e. the presence or absence of private industry in the respective environments.

In most situations I experienced a great deal of openness to my perspective as a sociologist/anthropologist, my use of qualitative methods and the goal of writing a monograph. During a university held course on obesity in which I took part, I met nurses from different areas of the Swedish health care system, such as primary care centres. In a discussion on how to deal with overweight patients one of them became very interested in using qualitative interview techniques in order to find out what the problems were from the point of view of her patients. At other times, however, my position as a social scientist was questioned. Was I a guest doctoral student at the department making a scientific contribution by studying the social aspects of obesity, or was I an anthropologist studying the exotic world of obesity care and research? And if I was seen as the latter, how is it that I could come and ask the staff lots of questions without having to go through the strict procedures of medical researchers in terms of ethics committees, *et cetera*, in order to conduct a research project? I

then had to explain that my research was not on patients, and that anonymity of the site and staff was guaranteed.

Problems such as these, that force us to understand each other's circumstances and premises for conducting research, are not a rarity when social and medical research cultures meet. The encounter does not always go smoothly. Intense debate about this issue in Sweden occurred when a Swedish anthropologist conducted a study on how women interpret the information given to them by their doctor in genetic counselling sessions (Sachs 1998). Sachs tape recorded conversations between a medical doctor and the doctor's patients during these sessions, and the conflict arose out of differences in opinion on how Sachs later analysed the data. The medical doctor did not agree with the analysis made by Sachs, and with reference to the "research subject's" right to withdraw from the study, she demanded that the recorded tapes be given to her. Sachs, on the other hand, made ethical considerations based on social science traditions, such as giving all actors pseudonyms, and she upheld her right, as the one doing the research, to interpret the data (Örn 1999). One reason why this conflict appeared is the differences in basic principles of research within different parts of scientific practice and in the difficulties in understanding each other's premises for conducting research.

With this conflict and debate in mind, I tried to be as clear as possible towards my informants as to what my conditions for being there were and believe I succeeded to a satisfactory extent. I was especially careful to discuss with Magnus the role he played in my fieldwork, since he had assumed the role of being co-supervisor. Indeed, he was a supervisor in the sense that he introduced me to the academic field of obesity research and the world of clinical drug trials. But he was also an informant in the sense that I interviewed him and analysed his accounts.

One final issue has affected the character of my data and, accordingly, the modifications of my research design. It can be characterised as the fluidity, or lack of stability, of the field. Project based employment is common within clinical trials, something which led to difficulties when I tried to do follow-up interviews, since several people had left the clinic. During the autumn in 2003, a year after my fieldwork was conducted and my first interviews done, the organisation of the clinical trial work was changed. Two thirds of the staff had to leave. Not only was the group of staff transient, but so were the drug studies themselves. Only a very small number of trials pass through the whole protocol due to uncalculated risks or side effects. Therefore, it is common that phase III drug studies shut down before all of the protocol has been carried through. In the Obe trials which I studied, a decision to shut down the trials was made in February 2002, during the first few weeks of my fieldwork. This also

affected my data collection in the sense that what the staff in the Obe trials were doing, once the decision had been made to shut it down, was “follow-up” visits with the participants, and not the routine visits I had thought I would be observing. Instead of studying the everyday work involved in routine visits which I would have done in situ, I ended up observing the ending process of a trial. To find out what the work preceding the shut down was like, I had to rely on interviews centred around the trial’s research protocol.

Doing field work in a clinical drug trial

Studying a clinical trial made me rethink the notion of what fieldwork meant. The field of a clinical trial spans several locales. In my case study, there is the firm PharmaCo and its staff, also the research firm SpinOff, which was managing the trial and recruiting patients, and the university ethics committee receiving the application from the “Principal Investigator”, who is the researcher responsible for the study. The field also included the university research department where the doctors responsible for the trial have their offices, their colleagues, and their coffee room. Finally – and most importantly for my study – there was the basement where the actual trial was performed, with the nurses, dieticians, clinical doctors and trial participants who meet over long periods of time. How does one do fieldwork in such a context?

Doing only observations is neither simple nor sufficient in this context, since the organisation of clinical trials involves a complex medical/scientific/industrial bureaucracy, has a culture of secrecy and includes important documents that need to be analysed and, at least partly, understood, in order to grasp what goes on. In my fieldwork I talked to a number of people who were involved in obesity research outside of the clinical trial, such as the head of a Swedish society for obesity, *Överviktigas riksförbund*, and one person at the Swedish Medical Products Agency. Mostly, however, it was the people involved in the trials that I interviewed. I asked lots of questions and we discussed issues which were central to both them and me. In the beginning, I tried to figure out how a drug trial was conducted and what the diverse new concepts I heard meant. What are audits? Who usually attends them? Why are jokes made about them? What are protocols and case report forms? How are they used in local practice? What does a monitor do? Are there any differences between research projects financed by the pharmaceutical industry and those which are not? Informal conversations around such issues were difficult both to remember and to summarise in later fieldnotes,

something that had to do with the detailed character of what I was learning. In this process I had great help from two handbooks for clinical trials (Jadad 1998, Lemne 1991/1997) that I continuously went back to when I needed to look up or review what it was that I had learned.

Therefore, my initial ambition to do traditional participant observation, as I knew it from my undergraduate studies in anthropology, had to be reworked. I had, first, to focus on being only in certain places since I could not get equal access to all places of interest. Secondly, I decided to try to get a hold of official documents and include them in my analysis. Finally, and perhaps most importantly, I came to rely on semi-structured interviews as my main method of collecting data (see Gusterson 1993: 63-64 for a discussion on the importance of interviews as part of participant observation). I did a number of tape recorded interviews around questions that had come up during observations and informal discussions

Fieldwork including interviews and analysis of documentary material was thus conducted in a Swedish university hospital department, from January 2002 to November 2004. I spent a total period of three months from January to June 2002 at what I will here call Centre University Hospital. During this time I observed the practices in the basement, spoke informally with the people working there, and conducted semi-structured interviews. I tape recorded interviews that I did with four dieticians, seven nurses, one computer scientist and six medical doctors. Out of these, seven were follow-up interviews that were done in late 2004 and included persons that had not previously been interviewed, in order to confirm parts of my analysis with the interviewees and to see if new concerns or patterns would emerge that I had not noticed before.

The department I studied is located in two different locales in the hospital area, in the research building and in a building which houses the clinical studies. In the research department, located at the far end of the hospital, one finds medical doctors, nurses, dieticians, administrators, biomedical analysts, one economist and one statistician. These are all involved in different research projects run by the department. The other, clinical part of my field, consists of a reception area and a basement, and is located in another area of the hospital. The basement is where the actual conducting of the drug studies take place. At the time of my fieldwork there were plans to reorganise the various research activities and put them all under one roof in what was referred to as an "obesity house". In total, there were around sixty people working at the department and clinic. Of these, around forty were involved in clinical trials. This number varies, however, depending on the number of trials being conducted. When a new drug study starts up or closes down, project based jobs come and go. At times

the activities have been so intense that the locales have not been large enough and new premises have had to be rented during brief periods of time.

During field work, my time was divided between the basement and the research department. I had my laptop installed in one of the rooms in the research department, where I used the office of the doctor responsible for the Obe trials, Magnus, my co-supervisor. He mostly used his office in the knowledge firm SpinOff, and was not at his office in the research department very often. I welcomed having a space of my own at times when there was no one around to talk to, no meeting to sit in on, or no interview to book or conduct. At those times I sat down and wrote about what had happened during the day. People did not really count on me for different activities, but I was informed about general meetings that I could attend. In the obesity department, such formal meetings included the monthly staff meeting and the one hour lunch seminar where different researchers presented their research. It was at one of these lunch seminars, during the early part of my fieldwork that I also presented my research plans. This was an important step in introducing myself to the different researchers at the department and giving all of them a chance to know what I was doing and to ask questions about the research. But it also manifested the double nature of my role there as a social scientist, double in the sense that I could be seen both as an outsider looking in on obesity research and as a guest researcher from the social sciences participating in an interdisciplinary department with a focus on obesity as a social issue.

After the introductory week I spent several weeks in the basement. I hung around during the day and tried to get a grasp of who everyone was and what they were doing. I initially did this by following the research nurse in the international trial, Ninni, for a day as she explained all the steps she did in the trial. It was not possible for me to follow everyone around everywhere, however. I could not sit in with staff when they met the trial participants since my research project had not been through the ethics committee. This made it difficult to get a grasp of the concrete doings of the staff and I came to rely on what staff talked about in the coffee room – the place where most of my interactions with staff actually took place.

In drug studies it is without doubt the patient who is the most important person. It is perhaps self-evident that all hospital practices are in place for the sake of the patient, but in spite of this, I have not included patients in the study, something that needs an explanation. At the beginning of my project I planned to look at everyone involved in the drug study, including the participants. At a very early stage I asked one of the nurses if I could have a few words with one of the participants present after she had finished her work. Then, when I talked to this participant it soon became clear to me that she did not distinguish between me

and the staff in the basement. I did not consider it ethical to continue this interview, however informal it was, as the interviewee in this specific situation could not really see that I was someone from another area of research doing something that was not really related to her individual participation in the study. Moreover, that day she had both been to see a doctor, a nurse and a dietician. In addition, she had been in the upstairs part of the clinic and placed in both a computer tomography machine and a DEXA. I was not comfortable in throwing more questions at her at this time. If I was to have interviews with participants it would have to be outside of the hospital setting, after their prior consent and with better information about the context of my interview. Such interviews would, of course, also have to be pre-approved by an ethics committee. I therefore decided to concentrate instead on the experience of the staff.

Perhaps more than other types of research, observations imply a need for reflexivity by the researcher. In this project where I have studied people doing research on other people (patients or participants), the issue of reflexivity has accompanied me throughout. In two particular areas where my analysis of how they deal with their research subjects, has directly influenced how I dealt with them as my research subjects. One is where one of my informants wondered how it was possible for me to do my kind of research on them, because in his case he would have to submit an application to the ethics committee, the Swedish Data Inspection Board, *Datainspektionen*, and “you name it”. How could I just waltz in and ask them all kinds of different questions? This made me, once more, think through how we as social scientists can deal with sensitive issues, since this is not as regulated or standardized as in the sphere of medical research.

The other area concerns what one may call the exchange relationship between the researcher and the research subject. My awareness of gift giving was partly triggered by the gifts given by the pharmaceutical companies to patients, nurses, dieticians and doctors involved in the drug studies, and the controversial nature of such gift giving. In one of the interviews I conducted I felt self conscious about booking a follow-up interview with the informant since she no longer worked at the clinic. I feared that she did not really want to go through this again and felt somewhat guilty because she had to see me on her free time. So, as a token of my appreciation I bought her a small and inexpensive symbolic gift. The interview circled around different issues, one of them being the “gifts” given to trial staff such as “start-up” meetings, including free meals and drinks in luxurious restaurants in major European cities. She did not feel the pharmaceutical companies’ practice of giving the staff such privileges was a good thing, and she had always been suspicious of the motives behind this gift giving. This remark made my comparatively small gift seem as a way of buying her time

and loyalty as well (and I did not want her to become suspicious of my motives), even though it was not in any way close to as expensive as dinner in a luxury restaurant, and since it was paid out of my own purse instead of a pharmaceutical company budget. This example nevertheless indicated that we enter into some kind of an exchange relationship as researchers. After the interview and assurances from my informant that she really thought it was “fun” to be interviewed, I realised that my gift had not been necessary. I was, however, reminded of my indebtedness towards her and all of my other informants for providing me with such rich and interesting data. It is something of value, not only to this project and for the sake of scientific research, but also as a resource for me as an aspiring researcher. So, in some sense, my small gift to this particular informant mirrors the larger gifts given to all my informants by the pharmaceutical firm. The similarities between the type of research I do and the type of research done by my informants, which is sponsored by a large pharmaceutical firm may not seem so big at first glance. But I have come to see the difference as one of scale and not of kind. In research there is no “knowledge on its own” since it is always also translated into resources for those conducting the research to achieve status, fame, or money.

My fieldwork has also involved analysis of various written documents. Examination of documentary material in addition to observations and interview material thus forms “part of a broader ethnographic examination of organizational settings, work practices, professional cultures and the like” (Atkinson & Coffey 2001: 269). First of all, and of greatest importance in this study, is the clinical protocol, without which the actions of the staff in the basement would be difficult to understand. To help me understand the terminology and general aspects of the clinical drug trials I have also frequently consulted a “Handbook in Clinical Trials”, authored by a medical doctor with great experience in the area. This made it possible for me to understand what the general way of conducting a trial is and what was specific for the Obe trials. Other documents around the practices of the Obe trials were also consulted, such as all documented communication between the ethics committee and the responsible doctor for the trial, as well as the risk/benefit report from the Obe trials that came out in June 2003.

Secondly, I have followed the debates and articles in *Läkartidningen* (the main Swedish medical journal) from 1990 up until 2003 on the influence of the pharmaceutical industry over clinical research and practice, on evidence based medicine and on the topics of obesity and obesity therapies. I have also analysed official reports and policy documents from governmental authorities. This I did in order to understand how actors outside of the hospital understand obesity as a diagnosis, and to understand who is for and against its medicalisation and why.

The limited character of my fieldwork, in terms of its reliance on data derived out of talking with people rather than observing their practices, was made up for by looking at other kinds of material. In order to understand how SpinOff's computer control system worked, I looked up the technical description of it in the application sent in to the World Intellectual Property Organization (WIPO). Similarly, I have analysed SpinOff's website to get another perspective of the firm than that I received from interviewing three people involved in the firm.

To contextualise my case study, I also attended a university course between October and December 2002 on obesity and its etiology (i.e. its causes and origins) designed for hospital staff from all over Sweden. The course consisted of lectures by leading researchers in the field about various aspects of obesity, its background, consequences and treatment. Moreover, it included a group project aimed at designing a plan of treatment for obese patients. Participating in this course and the group project made me aware of the way staff at diverse locations see obesity and what the problems in treating it are. It gave me a deeper understanding of obesity as a medical problem and how personnel from different parts of the health care system in Sweden view obesity and existing obesity therapies.

Interviews and observations

I interviewed persons involved either in the Obe trials or other drug trials that took place in the basement. In total I made 20 interviews (with four dieticians, seven nurses, six medical doctors and one computer scientist at the trial site, where two of the nurses were interviewed twice, once in 2002 and then again in 2004.) The interviews lasted between one to two hours, were semi-structured and focused on the interviewees' specific areas of interest and his or her perspective on the drug study. In the first round of interviews, I sent the transcriptions back to those interviewed to give them the chance to react to what we had talked about.

The information and viewpoints expressed in the interviews would not have been possible to get, had I not already become familiar with the workplace and the staff through my observations. Aside from the semi-structured interviews, I conducted many informal interviews about what people did and why, in the trial, and what they thought about it. Observing a situation is highly dependent on this kind of informal talk; the interviews and informal talk interact and enrich each other. According to Agar, the core of ethnography is the informal interview, while observation has a supplemental role (Agar 1980: 111). In my case

this meant that things which I wondered about or did not understand while observing were discussed in the interview situation. During my observations I learned who everybody was and what they did on a daily basis. Questions that surfaced through these observations I asked later in the interviews. And, conversely: issues brought up in the interview made me aware that many things were not visible through observing. In this sense the interviews and observations cross-fertilised each other. For example, there was nothing in the observations that suggested any kind of conflict or tension between health care and industry, something I was expecting to see. In a few interviews however, some informants voiced concern that certain colleagues had double loyalties or were “wearing two hats”, one being the clinic’s and the other being the knowledge firm’s. Without the interviews I would not have known that such opinions existed.

My initial observations, no doubt seen through previous and parallel reading of actor network theory, soon made me realise there was a non-human actor that had a great influence on the trial process as a whole, so great that I realised I had to find a way to give it substantial room in the study. This “actant” was the clinical research protocol, a lengthy document that acts as an extensive instruction booklet and guide for doctors, nurses and dieticians through every step in the clinical drug trial. It must be strictly followed in order for the trial to be done in an exact way and for it to be possible to coordinate what is done across the different trial sites. This document was not easy to access. On the one hand, it must be shown when the application to conduct the trial is sent in to the ethics committee. Since documents sent to ethics committees are official documents, I tried to get my own copy of the protocol after my observation period had come to an end. But, at the same time, the document is the property of the pharmaceutical firm, and thus confidential.

On the first page of the protocol, there is a confidentiality statement which states that the information in the protocol document contains trade secrets and confidential commercial information. The extent to which the protocol was confidential was not wholly clear, to me and others, which became obvious when I tried to access it. At the office of the ethics committee I was allowed to spend a day looking at the files concerning the trial, files that also included the clinical protocol. I flipped through these and decided the information was too condensed for me to understand then and there, so I asked if I could make a photocopy of it. The secretary was not sure if she was allowed to let me do this, due to the confidential nature of the document, and told me to talk to her director. The director and I had a discussion on what the difference was between sitting and looking at the document in an ethics committee office and taking a photocopy of the document with me. We came to the conclusion that it

was best for me to contact the pharmaceutical firm myself to ask them for permission. Doing this, I discussed what I intended to do with the information with the research head at PharmaCo. After the discussion about how to treat the confidentiality aspects of disclosing the information I was allowed to obtain a copy of the protocol. We agreed that it was acceptable as long as I did not mention the substance's name or the firm's name, and as long as I signed a confidentiality agreement, the same kind of agreement that all staff groups sign when working with a trial.

According to a lawyer at the Swedish Medical Products Agency, *Läkemedelsverket*, it is not surprising that the protocol is confidential since clinical trials sort under the EU directorate of enterprise and not the directorate of health (telephone communication in 2003). In other words, the protocol is to be seen as business material and not research material. Its confidentiality is supported by law, *lagen om sekretesskydd*. Apart from complicating my research, this showed how blurred the boundaries between business and research can be.

Analysing interviews, analysing documents

The analysis in this dissertation thus builds on different kinds of data: interviews and observations on the one hand, and written documents on the other. The transcribed interviews were continually reread throughout the research process. I made a rough coding or categorisation of common themes that came up in both the interviews, observations and informal talk. The research design became more and more specific during the course of data analysis. The notion of "data" is problematic, however. It implies that the (likewise problematic) notion of "theory" sits counter to "data", and that the latter is a thing out there for all to see. This is not the case, however, since no one can do exactly the same fieldwork as I did, and if they did, would probably end up with a somewhat different book. What one chooses to call data is highly dependent on previous knowledge of the field, research questions and perspectives derived out of earlier research and theory. It is therefore important to say something about how theory has informed my data collection, but also how my data made me choose certain theories over others. In this iterative process I did not separate time put aside for reading on the one hand, and collecting data on the other: during my work in the field I did not stop reading or thinking about what others have said about science, technology and medical practice. Rather, the readings and what my informants said and did were in a constant dialogue as I compared the different voices to each other.

As this dialogue progressed, I made a few important decisions in order to narrow down the broader issues I brought up in my research design. I can give two examples here of how my analysis progressed in this sense. A first decision which would have consequences for the analysis was to focus on the daily work practices of the women working in the basement: nurses and dieticians, a decision made partly from an early interest in making the everyday and seemingly mundane interesting (c.f. Smith 1988). This awareness of the importance of those at the bottom levels of hierarchies arose out of years of teaching and reading feminist studies of science and technology (such as Wajcman 1991, Cockburn 1983, Haraway 1991, Webster 1995), and were further triggered by remarks I encountered from several of the (often male) medical doctors. Even though they thought the work done by nurses and dieticians in carrying through the protocol was of utmost importance, some had difficulties in understanding why I was so interested in focusing on them. “Why? They only carry out the study”, one of them said. Such a remark implies a view of the nurses’ and dieticians’ work as being one of following orders and not being an active part of making a clinical trial work. As feminist research has shown, the invisibility of low status workers, in a hospital mostly women, reflects hierarchical organisations, which is also the case with clinical trials. So, I decided to focus on the work performed by the dieticians, research nurses and clinical doctors (all of them female except one) and explore the ways the gendered work organization took part in shaping clinical trial work.

Once this focus on women’s work had been made and I placed myself in the basement for observations, talk, and interviews, a second important decision was made. I did not really understand how the nurses and dieticians knew what to do all the time. This turned out to be because they followed the strict protocol for what they did. Also, in one of the drug trials, the Swedish trial, there was a lot of running back and forth to a computer located in one end of the basement. I realised that I had to have more knowledge about these information processing tools, something which I associated to actor network theory inspired research, where human and non-human actors play equally important parts in practice.

The data finally collected, which became the empirical basis on which this dissertation builds, consists of interviews, informal talk, observations and documentary material. In this data I have focussed on invisible work and the two tools involved in one clinical trial of an obesity drug – the Obe trial. Since the trial shut down at the start of my fieldwork I have not been able to observe the everyday practices involved in working with the Obe trials to an extent that would be ideal in order to fully understand how the personnel went about conducting the trial. Instead, I have relied more on what personnel said they did and how they

perceived of the work tasks and tools involved. This I have combined with analysis of the tools and their idealized way of depicting what is to be done. This work became a case study of how tools and practice together shape how the trial is conducted. As such, comparisons of other work situations involving standardized instructions and computerized management tools in clinical work can be done, and to some extent perhaps also in other work situations outside of clinical ones. The thesis thus contributes to a line of research on invisible work and rationalizing tools more generally and also contributes to increased knowledge about the processes whereby clinical trials are made increasingly efficient. Here, the computer control system plays an important part, as does the involvement of a private company, a contract research organization (CRO) in pharmaceutical testing. The role CRO's play in the Obe trials can be compared to how CRO's participate in pharmaceutical research and development more generally, something that has been called for in a recent article in *Social Studies of Science* (Mirowski & Van Horn 2005).

My fieldwork has involved interviewing people at different levels of the university hospital hierarchy. This means the character of the interviews differ from each other. Ostrander (1993) gives a few examples of such differences of her interviews with "elites" and "non-elites". Elites are used to being asked questions about what they think in particular issues and they speak at length and speak their mind or "just talk" (Ibid: 23), where the opposite goes for those lower down in the hierarchy. Such issues were evident in my interview situations as well. This led to the interviews being of different lengths. An interview with one of the doctors lasted over two hours, while an interview with one of the nurses lasted only thirty-five minutes. Another significant difference was the way different individuals related to the transcribed interviews I sent back to them to look over. One doctor wrote to me confidently stating that "what's been said is said", while one of the nurses was more self-conscious about what she had said, and was somewhat afraid of speaking out. Such issues affect the data that is the empirical base of this dissertation, which I have kept in mind while analysing it.

In the text that follows, all individual actors, the pharmaceutical substance, the pharmaceutical firm and the knowledge firm have been made anonymous. Every human and non-human actor bears a pseudonym, both for business confidentiality reasons and in accordance with social science ethical conventions. The pharmaceutical firm, here called PharmaCo, has agreed to let me to study a part of their documentation concerning the Obe trials, as well as consented to my being in the premises where the trials were performed. Giving the firm a pseudonym was a precondition to get access to the data. For the sake of

readability nurses' names start with the letter N, medical doctors' with a M, dieticians' with a D and the computer scientist with a C. The interviews are transcribed in Swedish, but the citations used in the text are translated into English. The excerpts are from the first round of interviews in 2002 unless stated otherwise. Italics are used in these excerpts to show when interviewees placed emphasis on what they said.

Introducing the Obe trials

Performing late stage clinical trials involves personnel, trial participants and financial resources on a large scale. The average number of participants included in clinical trials has increased, from about 1,500 in the late 1970's to about 4,500 in the mid 1990's. This number varies between different disease areas (Gassman et al 2004: 83). When it comes to conditions that a large part of the population displays, such as high blood pressure or obesity, the number of participants is likely to increase.

Coordinating the different tasks involved in clinical trial work is difficult in order to make the trial process flow in the same manner at different centres simultaneously. Given the amount of invested money at stake and the competition between pharmaceutical companies to find a new drug, the process needs to proceed as smoothly and quickly as possible. A number of measures are taken to discipline and localize the work and make the process more efficient. Before these processes are analysed, the case needs to be introduced: What are clinical trials? How many people are involved? These questions are important to discuss in order to understand the work and tools involved in the Obe trial, and to make the trial efficient and safe.

The Obe trials

The drug in focus in this book is Obe, a substance registered and used as a drug for another disease or "indication"⁶ than obesity. One known side effect in previous clinical trials of the drug was weight loss. Therefore it was decided to test lower dosages of Obe on overweight people, to see if, and at what dosage it would be safe and efficient enough to be used as a drug for weight loss. The purpose of these trials of the substance Obe is, in trial terminology, to evaluate its "efficacy" and "safety".

Since Obe was already a registered pharmaceutical product, it had already passed intense safety testing procedures. This means that it did not have to go through the early clinical testing phases again, and could start off with what are called "phase III" trials. Such testing of

⁶ Since the drug name has been made anonymous, this indication is, too.

an existing drug on a new disease is not uncommon in the production of new drugs. Side effects registered in the use of one drug (such as weight loss) are often turned into main effects to be tested on new conditions and diseases.

When I started my research, there were ten different trials being performed on Obe (see Figure 5:1), each with its own specific research question, all of which were testing risk factors related to obesity. In focus in this thesis are two of these trials: the international trial and the Swedish trial. The international trial included “well over 1,000 participants” and the Swedish trial around 540. These two trials were being performed at Centre University Hospital where I did my fieldwork. The international trial had its focus on the drug’s effect on obesity as the main research question, while the Swedish trial tested its effect on type 2 diabetes. Medical research has shown that type 2 diabetes is related to obesity. Therefore, it is important also to study the substance’s effect on this indication. Type 2 diabetes is defined as blood sugar levels above 7.8 mmol/L.

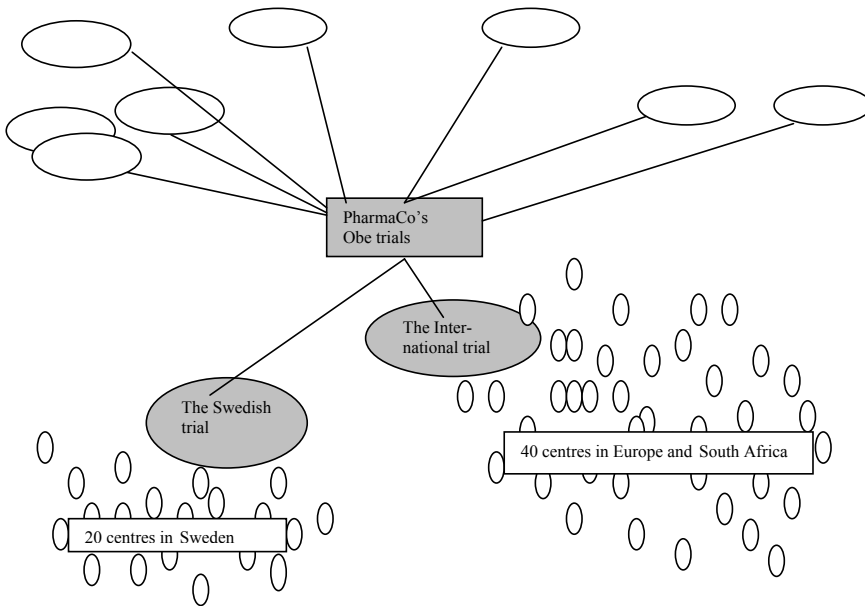


Figure 5:1: PharmaCo's ten different Obe trials

The international trial was a two-year international trial studying the long-term effects of Obe on obesity and was simultaneously performed in 40 different sites in (South) Africa and Europe. The Swedish trial, on the other hand, was a smaller one-year trial confined to Sweden, with 20 participating centres within the country.

In the Obe trials, the effect of the substance was measured against placebo. Within medical research, the use of placebo is sometimes considered unethical in the sense that it is not a treatment. The Declaration of Helsinki states that a patient who is enrolled in a trial has to benefit from participating, and receiving a placebo pill is not a treatment. The use of placebo is debated among medical researchers, especially in trials of obesity drugs, where existing obesity pills have only been shown to be a little more efficient than placebo (Hedqvist & Eggertsen 2002).

Today, multi-centre trials such as the Obe trials are being performed more and more often and can be performed at up to several hundred centres (Lemne 1991/1997: 54). Such large studies often occur in intervention studies, such as those of the preventive effects on diseases of the heart and arteries by blood pressure treatment. Other studies may be performed in more than one centre since it is sometimes difficult to enroll enough patients at one place within a reasonable time-frame (Ibid.). Multi-centre large trials are performed in the same manner as smaller scale trials, but the fact that many participants are involved makes some work tasks more difficult.

Performing multi-centre trials in the same way and at the same time in several different locations requires extensive coordination. One tool in coordinating these tasks across many sites is the clinical research protocol. It is a document that serves as a detailed set of instructions used by all different centres. Discussions often come up about how the research protocol should be organised. Routines vary between different centres, so they can all have different opinions on how to perform specific tasks. In international trials, this coordination process may be even more difficult since potential differences between different countries are likely to be greater than differences within one country. The problem of assuring that the tasks are performed in as similar a way as possible in all different sites is a recurring theme in Lemne's handbook as well as in the literature on clinical protocols (Berg 1997).

Large scale trials are very expensive and many are sponsored by pharmaceutical companies. PharmaCo is a research-based pharmaceutical firm with about 20,000 employees in close to 50 countries and with a yearly revenue of about 30 billion euros, and employs just over one hundred employees in Sweden. It owns the patent for the substance being tested in the Obe trials. PharmaCo continually checks up on how the work is proceeding through

monitoring the trials. This is done with the help of individual monitors who visit the trial sites at certain periods as well as through audits, when the firm sends a larger group to inspect the quality of the trial. Things that are inspected during an audit include how archives of data are stored, how informed consent obtained from trial participants is documented, how the drug is handled, as well as how original data is saved and made available and if this data corresponds to what is stated in the patient journal. According to Lemne (1991/1997: 63), this type of control is not generally performed at every centre. The more important a study and the more patients involved, the larger the control efforts of the firm need to be. Controlling and managing production across twenty sites in Sweden as in the Swedish trial, or across forty sites distributed in Europe and South Africa is an arduous task requiring coordinating tools, management strategies and an efficient organisation, something that will become more evident in chapter eight and chapter nine below.

Purpose and course of events of the trials

Both Obe trials are organised to study the “efficacy” and “safety” of the substance in question. The efficacy of the substance is measured differently in the international trial and the Swedish trial. In the international trial, it is measured primarily as the percent of weight loss accomplished throughout the duration of the study. Efficacy is also measured by taking into account other factors such as body circumferences, life quality, body composition and blood pressure. In the Swedish trial, efficacy is primarily determined by measurements of blood sugar levels.

Determining safety in both trials is done by looking into incidences of “adverse events” (i.e. side effects). All sorts of symptoms are taken into account, from toe problems to shivers and fevers to increasing liver enzyme levels. These symptoms are recorded, even when they do not seem to have any relation to the use of the drug. A data safety monitoring board, appointed by the firm but consisting of independent members, continually checks up on safety in the trials. In the case of the international trial of Obe, “serious and unexpected” side effects were discovered during the early course of the trial, and similar reports came in from the other ten trials as well. This eventually resulted in a simultaneous closedown of all ten trials at all centres worldwide.

This happened when the data collected from all ten trials was analysed by the monitoring board and it revealed a greater increase in liver enzymes in several cases, out of which two were considered “serious”. One was a case of fatal hepatic failure (i.e. liver failure) and the

other a case of toxic hepatitis (i.e. liver inflammation), according to the final report from the data safety monitoring board. After a meeting following these observations, held in the summer of 2001, the monitoring board suggested three ways to increase testing safety. One was to increase the intervals of liver enzyme testing in all centres in order to provide faster feedback, which would increase safety by enabling elevated levels to be discovered sooner. Another way to increase safety was to use a type of alarm system in the trial process, meaning that the central laboratory would alarm the principal investigator and the monitor when it read individual enzyme levels above a specific, previously defined, level. This would enable a quicker decision process as to whether to disengage the participant or not from the study. The third action to be taken was to evaluate the tests non-blinded and to involve independent liver experts in the relevant cases. These precautions were applied and a decision was taken to continue with the trials. Two more serious adverse events were later reported and became the focus of attention at the Monitoring Board meeting in December 2001. The first was a potentially serious psychiatric reaction and the second a small increase in serum creatinine and blood urea nitrogen, both of which are related to kidney function. These, however, were not considered acutely serious and the board recommended the continuation of the study but demanded further data collection prior to the next meeting in March 2002.

At the March meeting in 2002 the main safety concerns for all Obe trials were established as renal tubular acidosis⁷, neurocognitive effects, liver toxicity and glaucomas. In the specific case of the Swedish trial, there was one case of a participant developing glaucoma. This participant decided to end his or her participation in the trial. Another participant in the Swedish trial, who was registered as having an increased liver enzyme level in July 2001, later developed pancreas cancer with following metastases and was hospitalised in September the same year. This patient later died. It is, however, difficult in clinical trials to determine whether an unfortunate event such as this one is related to the drug studied, or not. Five categories are used in the Swedish trial protocol to judge the relationship between a serious adverse event and the use of the drug: “not related”, “doubtful”, “possible”, “probable” and “very likely”. The relationship between the liver enzyme increases and the cancer was considered “doubtful”. In none of the cases of serious adverse events in the

⁷Renal tubular acidosis is a disease that occurs when the kidneys fail to excrete acids into the urine, which causes a person's blood to remain too acidic. Without proper treatment, chronic acidity of the blood leads to growth retardation, kidney stones, bone disease, and progressive renal failure.

Swedish trial did any doctor judge or report a “possible” or stronger connection between a reported event and the drug, according to the monitoring board’s final report.

The persistent high liver enzyme levels as well as the incidences of glaucoma finally prompted the Monitoring Board to decide to shut down all the Obe trials. This decision was made in February 2002. The trials were then terminated over a period of six months and only one of the trials was “completed per protocol”. As for the international trial and the Swedish trial, they were shut down before all visits in the protocol were performed – they were not finished “per protocol”. From what could be seen in the results gathered, the monitoring board came to the unanimous conclusion that Obe was “highly effective” and had “acceptable” side effects for the groups who received the lower dosage of the substance. It was effective when compared to the already existing drugs Reductil and Xenical, meaning it produced roughly five to ten percent weight loss. Also, preliminary results showed that the visceral weight loss was higher than the total body weight loss, which meant efficacy in terms of a decrease in diabetes incidences. The monitoring board ended its report by strongly urging the firm to continue the evaluation of the substance as soon as possible. Future Obe trials would not include the higher dosages with the unacceptable safety profiles, and it is suggested that the most serious side effect, suicidal ideation, could be addressed by “appropriate labeling”.

Shutting down the large scale Obe trials did not mean that the whole study was a failure. A substantial number of participants did lose considerable amounts of body weight; something which led the data monitoring board to the conclusion that new trials on the substance should indeed be made. By going through the vast amounts of data which had been gathered worldwide, it would be possible for the firm to exclude future participants with similar characteristics to those who had displayed the trouble with glaucoma and liver enzyme levels that eventually lead to the termination of the trials. Thus, Obe may still have a future as an obesity drug.⁸

⁸ When this book goes to print, an application has been made to conduct a follow-up study using pharmacogenetic methods to determine the genetic differences between those who had side-effects with those who did not.

The international trial and the Swedish trial

Having given a background on the large scale Obe trials and their main goals, it is now time to narrow the focus to the international trial and the Swedish trial: the two trials of Obe being performed at Centre University Hospital where I conducted fieldwork. The Swedish trial started simultaneously in all clinics in January 2001. It was run from the obesity department at Centre University Hospital by the Principal Investigator, a professor at the department. It was a trial with 541 enrolled participants, distributed through 20 different clinics in Sweden. To participate in the Swedish trial, participants had to have a body mass index of between 27 and 50 (roughly a person with a height of 170 centimetres who weighs between 78 and 145 kilos), together with previously undiagnosed or untreated type 2 diabetes. The Swedish trial has a special place at Centre University Hospital obesity department since it is run by its head of the department, whereas when it comes to the international trial, the Centre University Hospital is just one centre among others.

Both trials were “phase III, randomised, double blind, placebo controlled, multi-centre, parallel group, dose-response” studies. This means that the participants were randomised into different control groups (three for the Swedish trial and four for the international trial), where one group received placebos and the other groups received different dosages of the substance. The term “double blind” implies that neither the administering nurses and doctors nor the participants knew which strength of the substance the participant was receiving. This is to minimise the risk of nurses, dieticians or doctors treating participants differently depending on what group they are in. In practice however, it is difficult for the nurses and doctors not to have an opinion on whether the participants are in the group with high or low dosage categories respectively. The amount of weight that a participant loses is evident and several of the staff I have talked tended to assume that when a participant had been very successful in losing weight, this weight loss was due to the pill having an effect.

The very scale of the Obe trials, involving both thousands of participants as well as health care staff in many parts of the “westernized” (read wealthy) world, makes evident the need for organising, and coordinating the endeavour, especially if the results from different places are to be compared and analysed centrally. This is where the detailed and extensive research protocol and a computer system aiding the recruitment of patients have an important function together with the local practices. The protocol and the computer system will be described in detail in following chapters. However, in order for such detailed description to be better understood, the practices of the international trial and the Swedish trial will first be

situated the local context of a university hospital in Sweden. This allows an analysis of the tensions between the universal plan of the trial – the clinical research protocol – and the practices of the local participating centre. I here refer to the tensions evident between the universal and standard plan in the protocol, formulated as a tension between a standard, and the work of local staff (Star 1991a, Berg 1997). This tension can also be said to be one between “science” and “care” (Meuller 1997).

The protocol in the respective trial is the same one used in all participating centres, be they in Sweden, the rest of Europe, or South Africa. It would be interesting to compare the uses and meanings of the protocol between different locales, but that is beyond the scope of this book. Instead, the focus here is on how the protocol is localized and made to work in Centre University Hospital in Sweden.

Local topography of the Obe trials

The department in charge of the Swedish trial, which was also hosting the international trial, was located in two different parts of the hospital. One locale housed the research part of the department and the other the clinical part. The staff working on research projects moved freely between the two locales while the clinical staff seldom, if ever, were seen in the research department.

The actual trials took place in the main building of Centre University Hospital, in the health clinic. The health clinic was divided into two parts, one at the ground level, and one in the basement. Upstairs in the clinical unit, patients were referred to a doctor, nurse or dietician for their condition, while the basement was where participants in drug trials went when they were due for their visits.

The division of the clinic into two parts was done when one of the first large clinical drug trials, was started. The scale of this first project required more space than was available in the clinic, so possibilities of expanding the clinic were examined. The basement under the clinic was remodelled from a run-down storage area into office spaces, consulting rooms, a coffee/lunch room, lab room and conference room. This renovation was paid for by sponsorship money. Keeping the activities of the upstairs clinic and the basement drug trials separate served not only the need for extra space to start with the study. Another function the division served was to keep publicly funded health care separate from private industry drug trials, something that the professor of the department said he saw as a way to prevent discussions around where the boundaries between private and public interests go.

When participants came to the trials they were measured in a great number of ways, something that will be explained in more detail in chapter seven. There are many ways to measure the amount of fat in the body, and several are used for the clinical trials at the department. Simple and inexpensive methods are used parallel to expensive and advanced technological equipment. The latter are located in the upstairs part of the clinic. One of the more expensive pieces of measurement equipment was the DEXA (Dual Energy X-ray Absorptiometry), a low radiation device that measures how much of the body weight is located in the bone structure. There was also a computer tomography (CT) scan used to see how much of the body fat is located on the inside of the abdomen and outside. Three radiology nurses worked full-time with the DEXA and CT scanner. There, both “academically initiated” (i.e. non-drug studies) as well as “clinical” practices took place.

Downstairs was where the clinical trials of new substances against obesity were conducted. Unlike the patients with a referral to the clinic upstairs, the participants in these trials went directly down to the basement when they were due for their visits. The people working in the basement consisted of nurses, dieticians and one secretary. All of them were directly involved in the clinical trials funded by pharmaceutical companies. Nancy, the administrative head of the clinic had her office upstairs, as did the only “bedside” doctor of the department, Mikael.

Around sixty people were employed at the department, out of which approximately fifteen worked in the clinic and the rest in research. The research department was located in a different part of the hospital area. There, several other academically initiated research projects were being conducted by dieticians, nurses, economists and psychologists. Thus, most employees at the time of my study worked with drug trials. These figures can be compared to the number of visits that were related to research and health care respectively. According to the clinic’s own public information, the number of clinical visits (be they visits to a nurse, a doctor or a dietician) were 6,800 during 2002, while research visits were 4,400. The clinical visits were divided into 1,400 visits to a dietician, 2,200 doctors’ visits, and 3,200 nurse visits. Of the 4,400 research visits, some were drug studies and others other research projects. The amount of time given to the drug study participants, however, is far greater in a drug study than that given to patients coming to the clinic by referral.

Another site where people did work related to the Swedish trial (not the international trial) was at a university based firm, SpinOff, which managed certain parts of the trials, especially the arduous task of recruiting participants. SpinOff is located in yet another part of the hospital campus area. The firm is mainly involved in tasks related to the management of

huge amounts of data, but also other tasks oriented towards making the screening and recruiting processes less time-consuming. This firm started as a spin-off from the department/clinic using the software developed to handle data in one of the largest clinical trials performed at the department. It became a private firm since dealing with large amounts of data was not considered part of the hospital's duty, and also because it seemed to be a good business idea. Therefore, some of the researchers and engineers employed at the department took the opportunity to commercialise their work. The firm started with two engineers, a medical doctor and the professor at the department. It employed around thirty people in 2001, when the Obe trials were conducted, out of which four were nurses who had previously worked at the Lab. Since this firm plays a large part in the Swedish trial, chapter six will describe in greater detail what it does, as well as the tools it uses to do it.

Staff in between care and research

The doctors at the department worked with research and care to varying degrees. One doctor worked exclusively at the clinic and was not involved in research, but most doctors at the department were involved in research to some extent, some more than others. All of the doctors, however, still receive patients at least one half day per week, even though it is difficult to combine research and care according to one of the doctors. Most of the doctors are also involved in the planning of future research, including work tasks such as reading protocols and handling negotiations with pharmaceutical companies. This background work for the studies prevents their working "on the floor" to a greater extent. The division of labour between doctors is indicative of the polarisation between care and research seen in many academic hospitals. "Nowadays, it is not possible to be a bedside doctor and a paper researcher at the same time", the clinic's doctor, Mats, told me. Another doctor at the department, Mikael, agreed that the background work for research has taken away more and more of the traditional doctors' work.

The person formally responsible for the Obe trials at Centre University Hospital, the so called principal investigator, was Markus, who was the professor at the research department. In practice, though, it was another doctor, the co-principal investigator, Magnus, who oversaw the follow through of the trial. Magnus worked mainly at SpinOff, but had one half day per week at the clinic included in his job description. He was previously employed full time by the department. Magnus' goals and interests, as far as the Swedish trial was concerned, differed a great deal from those of the study's research nurses and dieticians. Magnus' pay

check originated from SpinOff, not from the department. Magnus was, in addition, planning a move to a foreign country to be part of the establishing of another office for SpinOff.

Aside from the doctors, there were also nurses and dieticians working in the trials. Ninni and Denise worked together in the international trial, and Nora and Diana worked with the Swedish trial. There was also a doctor in each trial in charge of the regular physical examinations and also responsible for the reporting of serious side effects or other medical issues that came up during the trial.

All staff groups involved in clinical drug trials cross the boundaries between “care” and “research”. Part of their research and administrative practices involves meeting and discussing with pharmaceutical companies, “sponsors”, about future and ongoing co-operations. The doctors’ different roles require different presentations of their selves, something which was evident in which clothes research doctors were wearing in different situations. When the sponsors were visiting, the doctors meeting them were wearing suits and ties. This phenomenon was something that other groups of staff sometimes mildly joked about, and in such a situation Magnus was jokingly called “the director”, for example. But, on an everyday basis the clothing style was more casual, and predictably, the doctors put on a white coat over their everyday clothes when meeting patients.

Clinical drug trials at the department are referred to as “drug studies” and the term “trial” is rarely used. Other terms from the pharmaceutical industry have, however, entered into the practices of the department. One such term is “sponsor”, which is used for the pharmaceutical firm that pays for a trial to be conducted, no matter on whose initiative the study was started. The term may seem inappropriate since it often is the pharmaceutical firm that has asked for the study to be conducted: the trial is commissioned work. Given the lack of funding for academically initiated research, however, the term seems more logical. In fact, due to the difficulties of receiving non-industry funding, the pharmaceutical industry serves as a sponsor even for non-pharmaceutical research, since it enables purchases of expensive equipment that can be used in other, internally or academically initiated projects. It is difficult to get funding for basic research at the obesity department, as in most university departments today. A number of such basic research projects are conducted with some funding from research councils but not enough to keep them afloat. It is no secret that the funding from clinical trials spills over into basic research projects at the department. This makes clinical trials important to the department’s finances as a whole. The relationship between academically initiated and industry initiated research is an unequal one in terms of both scientific status and financial resources. Drug trials are to a lesser extent seen as research, as shown by the way some

researchers make a distinction between “drug studies” and “research”. Clinical drug trials serve an important function in the clinic and department, however, not only because they imply funding that spills over to the departments’ own research but also because they give trial staff different kinds of fringe benefits.

The boundaries between what counts as public health care and a private drug trial is not a clear one and it could be a boundary that is under reconfiguration (Clarke et al. 2000). Persons from different staff groups show ambivalence as to whether the drug studies are “pure” research or if they could be seen as health care, or at least part of health care. Nurse Natalie expressed such ambiguity through the following statement:

It is a study. It is. But you can say care is included in it.

(Natalie)

The science/care dilemma is here also evident in the clinical trial, but it is articulated differently by different doctors, depending on how involved the doctor is in the study. Medical doctor Mikael talks about health care, not as something that is part of the drug study, but as something that takes “the shape of research”. Another doctor, Maria, who at the time was not involved in a research project except that she conducted some of the physical examinations in the international trial, said her engagement in the international trial was low, and that she was more interested in the participant-patient’s health and progress in losing weight on a clinical level. She stressed the fact that she saw herself primarily as “the patient’s lawyer” and doctor. But she was aware that she was able to focus on these clinical aspects because she did not have to consider how much money the department was to get or how well the trial staff was following the protocol. From the way Maria stressed this, it seemed as if having substantial responsibility for these latter aspects of a trial also meant not having the patient’s clinical needs as a first priority.

In this chapter I have indicated that organising and conducting a clinical trial is a large scale endeavour, both in terms of financial cost and geography. Tasks have to be coordinated across trial sites as well as within each site. Like other industrial processes, the trials need to be standardized and made efficient in order to keep up with increasing competition in the pharmaceutical industry. Extensive coordination is needed between the different centres as

well as between the research organization of the trial and the local clinics where they are performed, a coordination that can be seen as also coordinating between private industry and public health care. Given the safety aspects of all clinical trials, the efforts to organize and standardize such cooperation have to be done in a way that does not endanger the participants' health or be unethical in any other way. Parts of this organization and management have become a business niche that is sometimes referred to as "the clinical trial business". In the next chapter, I will describe one knowledge firm involved in this kind of work, the company SpinOff, and analyse its character and role in the Obe trials.

Rationalizing tools I:

SpinOff and the role of a large database and computer control system

Within the clinical trial industry – as in many other areas of production – there is a strong and increasing trend to outsource work tasks. The development of auxiliary professions and firms to support pharmaceutical production is in line with this trend. Such auxiliary firms include contract research organizations (CROs), site/study management organizations (SMOs), clinical trial advertising agencies and central patient recruitment companies. This chapter deals with one such auxiliary firm, namely SpinOff, which manages one of the Obe trials in this study, and which straddles the boundaries between these types of auxiliary firms.

SpinOff develops and sells services and software for the planning and follow-through, or what they call realization, of Phase II to IV clinical trials. Its clients are pharmaceutical companies such as the sponsor of the Obe trials (i.e. the firm who owns the patent for the drug). SpinOff is involved in the trials from the early planning stages to the end when the data has been collected and the database, where all study data concerning the trials are collected, is closed down. Its main contribution is to reduce the time needed for recruiting patients, something often considered a bottleneck in the clinical trial process.

In this chapter I will describe how this auxiliary firm was started and what its main areas of work are where the Swedish trial is concerned. In later chapters a comparison is made between the content of clinical trial staff's work tasks in the Swedish trial (where SpinOff was involved) and the international trial (where it was not). The description of SpinOff in this chapter serves to situate the computer control system that they have developed and which is the central innovation of the firm. I will then go on to analyse what this computer system does in terms of rationalization of recruiting, selecting and scheduling trial participants.

The pharmaceutical industry is sometimes said to be in a state of crisis due to decreases in productivity (Gassman et al. 2004). Part of the way in which the industry tries to make production more efficient is through managing and standardizing the work tasks performed by clinical trial staff groups, and through increasing the control over those performing them. The

use of the firm SpinOff's computer control system, to be discussed in this chapter, is a way to do all of these.

A short history of SpinOff

The proposal to form the firm SpinOff was made in 1999, and it was registered at the Swedish Patent Organisation by the end of that year. Official commercial activity started in February, 2000, and at the start it employed five people. By the end of 2002 that number had reached thirty-three.

SpinOff, and related kinds of firms such as CRO's, SMO's or as one informant called them, CRP's, clinical research partners, all fall under what economists refer to as knowledge intensive business services, KIBS. One description of KIBS reads:

KIBS are special services. They are specialists in solving their clients problems. KIBS firms are business firms (i.e. not governmental organisations) which provide knowledge-intensive, technology based service products with high levels of supplier-user interaction that are produced by firms employing a highly educated labour-force. (Nählinder 2002: 23)

SpinOff fits well in this definition. The business idea of SpinOff is to sell services that shorten the time it takes to conduct clinical trials and simultaneously produce higher quality results in terms of more reliable data. Producing such results also implies managing and controlling the staff involved in clinical trials to help them perform the work tasks in the manner and time frame specified in the clinical research protocol.

SpinOff was started by two computer scientists who previously worked in the hospital clinic together with two doctors who still work at the department. The idea behind the firm arose out of a need to deal with the increasing amount of data that a previous large clinical trial had generated. The general goal of the firm was therefore to develop software to handle such amounts of data and develop new methods to make clinical trial processes more efficient.

Phase III and IV trials are large scale, costly and run over long time periods. A phase III trial can take up to three years to perform. The most time consuming part of such a trial is often the recruitment of a homogenous group of participants. The participants have to meet the specific characteristics needed for the trial in question and need to be a homogenous group in other aspects as well (defined by a number of criteria in the clinical protocols) in order for

the potential effects of the tested substance to be compared. In the Swedish trial, the participants were to have previously undiagnosed diabetes and a BMI between 27 and 50.

Another problem in clinical trials is the fact that a certain number of participants tend to drop out during the trial. Researchers are often overly optimistic about how many participants will decide to continue the study, but a general rule of thumb suggests that the final number of participants will be reduced to 10% of the original estimate, something popularly referred to as “Lasagna’s law”, after one of the pioneers in clinical pharmacology. In a commentary in the *British Medical Journal*, assistant editor Sandy Goldbeck-Wood noted:

Only hindsight allows confident “prediction” of the likely rates of outcomes or of numbers of participants recruited, and similar difficulties must have been faced by many researchers. (Goldbeck-Wood 2001)

Therefore, the planners of large scale trials are faced with the problem of ensuring they have the required amount of people needed at the end of the trial process in order for the study to be deemed statistically significant. The investigator has to make an informed guess as to how many participants should be screened in order to end up with a sufficient number of people at the start of the trial, and then, preferably, with a drop out rate as low as possible.

It is by solving the problems of recruiting the right amount of patients, doing it in a short time, and still keeping a low drop-out rate that SpinOff has become successful. The main business idea of the firm is motivated both by the existence of a scientific, methodological problem, and by the economic necessity of ensuring that the trial goes as predicted.

SpinOff was formed out of the work with software developed during a previous large scale research project at the obesity research department. The computer scientists and doctors involved in this work on the previous study soon realised that the software being developed at the department had commercial potential and could be used in other upcoming large studies. Previously, the managing of recruitment and scheduling of trial participants was done in the basement by clinical trial staff (mainly research nurses), a work task that became computerised. By introducing a computer system that each nurse at every centre could enter data into directly, the work required less staff in the basement. Thus, certain parts of the management of the trial were moved from the basement staff to SpinOff. How this rationalizing tool is localized into the work in the basement is discussed in more detail in chapter eight.

The reasons for the commercialisation of the recruitment and scheduling tasks in clinical trials were several. According to Mats, the doctor who was the principal investigator of a

previous large scale study and a stockholder of SpinOff, it was not primarily done to “have a good cash cow” for the obesity research at the department. According to Mats, money was not the issue. Rather, commercialisation of computer tasks was done to make it easier to recruit the “talented engineers” needed in order for the work to be done. This recruitment, he points out,

...was during the time when the IT sector bloomed and the hospital was prepared to pay 25 thousand [Swedish crowns] when the gentlemen could get 40 in Ericsson. So that was pretty much the driving force. It was a practical solution to a problem. And then it turned out it was a commercially very negotiable idea. But I don't think anybody had that feeling when we were putting forward the system for [previous clinical trial]– it was rather a genuine spin-off, you can say.

(Mats)

Keeping the computer scientists in the hospital and not going in to the IT business was, thus, the main reason given for starting up SpinOff. The computer scientists would thus make the kind of salary they could get by working in a private firm and thereby stay with the clinical trial work.

The funding needed to start up the company came partly from a pharmaceutical firm that had conducted another drug trial at the clinic. This funding enabled what Mats referred to as “tens of man-years of programming”. The pharmaceutical firm that was the “sponsor” in the above mentioned study was offered a share in SpinOff as a “thank you” for the resources they had put in. But the sponsor declined the offer. The reason for this, according to Mats, was that it did not think the software part was something that it should be doing as a pharmaceutical firm. Software development and IT was not seen as strategically important for them.

The start-up of a knowledge firm gave advantages not only to the individuals who were part of it, but also to the university in terms of fees paid by the firm. Moreover, it is also said to benefit the region by providing job opportunities. The status of a knowledge firm is not wholly unproblematic, however. In SpinOff's case, agreements had to be made and contracts signed relating to the firm's use of the hospital's equipment, staff, premises, computer network and databases. Contracts also had to be signed as to how the firm would be allowed to use the term “a knowledge firm at Centre University Hospital”. A certain percent of the firm's profit is returned to the department at the university hospital as compensation for use of this designation.

There is also a difference in norms between a private company and a state authority such as a university. These differences in norms can potentially create friction and conflicts of interests between the university and knowledge companies, according to a document published at the university hospital discussing the making of rules for the relation between companies and the Centre University Hospital.

The starting up of SpinOff created another dimension of the relationship between public health care and the pharmaceutical industry, something that became evident in my study by some confusion on the part of the clinical trial staff as to SpinOff's role in relation to them. The confusion seems to be partly due to their superiors suddenly wearing two hats: one from the (public) research department and one from (privately owned) SpinOff.

Of relevance here is the Swedish "teacher's exemption", where the patent of an innovation made in a university is owned not by the university or the department but by the individual researcher as in many other countries. In the above mentioned document on rules and guidelines for knowledge companies, the university presents the starting up of knowledge companies, with their collaboration between industry and research, as something beneficial to all parts. But the university also sees risks with such collaborations: resources may be concentrated on running a business at the cost of other activities. The teacher's exemption can thus create certain conflicts of interest between the university, the researchers, the researcher's firm and private industry.

The staff in SpinOff

The firm is involved in all the phases in the Swedish trial, from the recruitment of participants, via the screening of the "subjects" and to the follow through of the study. Contacts between the clinic and SpinOff are close and the boundaries between them are not always sharp. The co-principal investigator in the Swedish trial, Magnus, has an office in both the clinic and in SpinOff and some of the firm's employees have been recruited from work with trials in the clinic. SpinOff has its office in a building in the university hospital area, which also enables close contact.

According to the firm's annual report from 2001, eleven persons were then working with systems design. In addition, there were four trial management nurses, one mathematician, one global R&D director, one president, one president's assistant, one medical director/vice president, one project coordinator, and one process developer. The global R&D director, Magnus, the president, two of the trial management nurses and the head of software design,

Calle, had previously worked in the research department or in the clinic. Before that, Calle worked for the mobile telephone industry. He started working in the obesity clinic when the contract for the previous large scale study had just been signed. His knowledge and experience from working with software development and with certain computer languages and his knowledge about how to structure relation databases were needed in conducting large scale studies.

Calle was part of the start up of SpinOff, together with another computer scientist from the clinic (now the president of SpinOff) and the two doctors responsible for the preceding study (the co-principal investigator and principal investigator). Calle and the other computer scientist now work full-time in SpinOff while the two doctors remain in the obesity department. The doctors are still involved in SpinOff, however, through being members of the firm's board and shareholders.

The firm has trained four trial management nurses, TMNs, who during the the Swedish trial travelled around the country and controlled that the trial was performed in the same way in all the twenty centres. Two of these nurses were recruited from the department. SpinOff's efforts to make the trials more efficient in the Swedish trial can be seen to mostly affect and be aimed at the nurses and dieticians working in the basement.

As a fledging firm being able to pay higher salaries than the hospital, SpinOff has had success in recruiting what they consider the best employees from the hospital. In Calle's words:

... we've had the possibility to hire people with a certain amount of experience and we've been able to freely choose people that we've worked with before and people we know. So we've been able to hand-pick people with good communicative abilities and a wider area of interest.

(Calle)

The hand-picking does not only involve computer engineers. One of the things that are frontlined both on the firm's website and by Calle is that the firm has competencies within a broad range, not only in computer science. This mix of competencies is, according to Calle, what makes SpinOff successful. Calle divides the staff into three categories:

First there is the management side... the nurses who know how this really works, who can meet the patient well, and who are professional in their demeanour. And then there are the doctors who are good on the theoretical medical side. And on the technology side is us, who are pretty good at what we're doing. Pour and stir... it's pretty fun actually.

(Calle)

The idea of SpinOff seems to create a happy mix of clinical staff, researchers and computer engineers, each providing what he or she is best at.

SpinOff is not the only auxiliary firm involved in the Obe trials. Two contract research organisations (CRO's) are involved in the Swedish trial. One (not to be analysed here) deals with certain confined work tasks such as the analysis of the electrocardiograms being taken. Another does the monitoring of the Swedish trial. There is no site management organisation (SMO) involved in the study, but SpinOff can be characterised as being more an SMO than a CRO. An SMO helps a sponsor with its documentation of clinical trials according to all rules and its contacts with a certain hospital or indication area, often meaning access to patients and access to various hospital resources and networks. In that sense SpinOff could be seen as a form of SMO. But, Calle does not want it to be categorized this way. Instead he used a new term, a clinical research partner, and defines it like this:

...we've had great difficulty in defining ourselves. What are we? Well, we're not a CRO, we're not a SMO. So what are we then? A clinical research partner is the best I've come up with: CRP. By this we designate ourselves as solving not just the small particulars, like "give me a small scrap to do and I'll do it without paying attention to the whole", because what's interesting is the whole. We're more a partner to discuss with, like "how could we do this differently"?

(Calle)

How SpinOff wants to be portrayed publicly can be seen on the firm's website and in their promotional material. SpinOff has made use of a well renowned advertising agency to shape its public image. The brand name of SpinOff is well thought through, as well as the images they use, which show highly concentrated people in modern office environments as well as with the latest computer equipment. Icons of modern science and technology, such as test tubes, a measuring tool and pills, also figure in their promotional material.

The firm's annual reports are designed in a similar way as the website. They can be downloaded from the website and contain images of all the employees doing their work with

expensive scientific equipment, or sitting on horseback, or engaged in martial arts. The images also convey a sense of direction. One image portrays a man standing on the left hand side of the picture and pointing his right hand towards the sky. Another recurring image is one of a solid staircase, giving an impression of an upward direction. A third image pictures a boot-clad foot just taking a step on the gravel, an image that can be seen as an analogy of taking the first step on new land, or on the moon. From these images one gets the impression that the staff of the firm consists of healthy, up-to-date, friendly and active people. The images signal that the people and the work being done at SpinOff is part of the business world rather than of the public sector – imagery shared with other high-tech companies.

This promotional material is geared towards the potential clients: the pharmaceutical companies. The material seems designed to show them that SpinOff is an up to date and efficient partner that will help them make their clinical trials quicker and more efficient by optimising resources and being able to control the trial process. This promotional material, however, lacks images about the specific health problem that the firm is involved in, namely obesity. No overweight bodies are to be seen anywhere. This is interesting considering that the overweight persons who have agreed to be in the recruitment database are one of the firm's main assets. One fuzzy image portrays an anonymous mass of people in a street. This gives a sense that the firm does not specialise in any specific type of patients, but that it can help its customer find the right homogenous group of people, no matter what kind of patient the sponsor needs.

Recruiting participants

The outward image of SpinOff shows a mixture of different types of competencies, those of nurses, doctors and computer scientists. When looking into what the firm does more concretely, a slightly different picture emerges. Here, the engineering perspective dominates. As we have seen, most employees work with computer programming and these are the ones Calle proudly referred to. SpinOff's main tool is the computer software system mentioned earlier. The software system and the database of SpinOff are based on the system made for a previous drug study, before SpinOff was started up. This system, in turn, was based on previous experience from working with another even earlier drug study. Mats, who was the co-principal investigator in the previous study and board member of the firm, describes the work performed by SpinOff in the following terms:

You can say that we refined principles for logistically controlling a large study. Principles that had developed from [a previous trial] and that cross-fertilized with experiences that our two engineers brought with them from the industry they came from [automobile firm and cell phone firm].

(Mats)

What SpinOff did was to take a production process perspective developed in the automobile and cell phone industries and apply it to the clinical trial process. The principles for rationalizing the production of cars and cell phones were applied to the production of clinical research data. This production can be described as follows:

As a first step, the clinical trial participants, the metaphorical raw material for the production of data, have to be recruited and selected. The participant group in a clinical trial has to be homogenous so that variations in how individuals react to the substance can be compared. Producing such a homogenous group involves a substantial amount of planning and organisation. In the Swedish Obe trial, an estimated 541 participants were needed. Finding them was not an easy endeavour as the trial's clinical research protocol has a long list of inclusion and exclusion criteria making a substantial part of the willing participants unsuitable for further participation.

In many clinical studies, to find participants is considered the Achilles heel which can take up to one and a half years. The traditional methods to get in contact with potential participants in clinical trials such as the Obe trials have not traditionally been systematized in any way. Doctors at different centres would keep their eyes open for potentially interesting and interested people, which could take a long time. What SpinOff has done in the Swedish trial is to make this recruitment and selection process considerably faster. Estimates were made as to how many willing participants were needed to be screened in order to end up with the right 541 patients. The conclusion was that the 35,280 people (see Figure 6:1) would be needed in order to finally arrive at the 541 eligible research subjects.

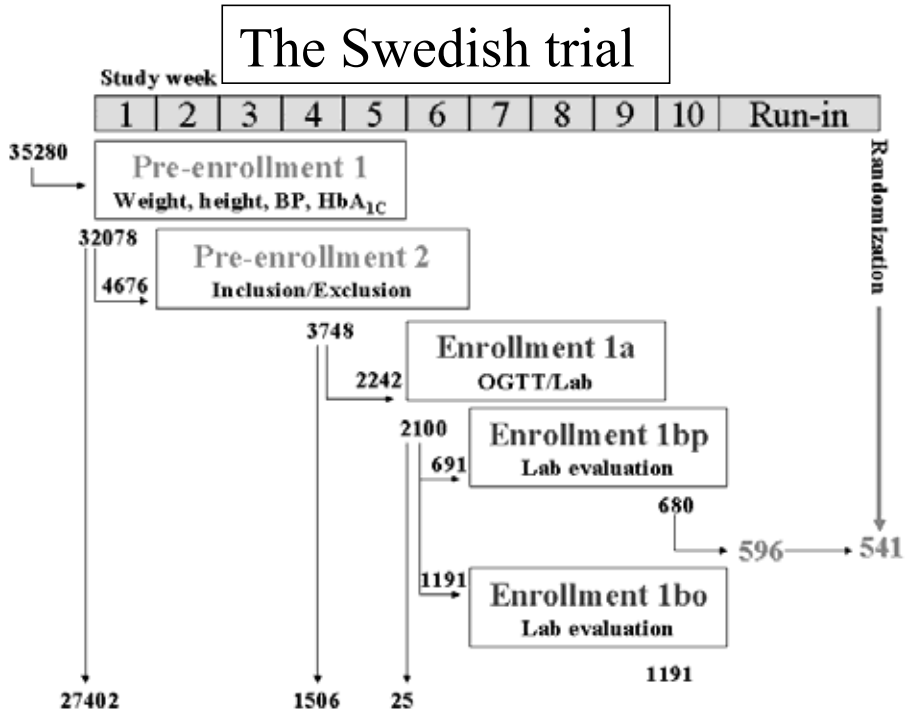


Figure 6.1: Recruitment and selection of trial participants. Figure provided by co-principal investigator Magnus

In order to find these 35,280 individuals SpinOff started a massive recruitment campaign through advertisements in newspapers and on television as well as through a small brochure with the title “If you are overweight”, which provided brief information about what to do if the reader wanted to participate in a pharmaceutical study. Reporting one’s interest was done by sending in the paper slip provided, or via a specified homepage. By doing this, the applicant also agreed to have their details saved in the database for use in other trials. The information given by potential participants was body weight and length, whether or not they had diabetes, and information on medication they took on a regular basis.

The television commercial was aired in October, 2001 on Swedish television and depicted two doctors in white coats running around in a residential building knocking on apartment doors in search of participants. At the end of the commercial, there was a text explaining what to do if the viewer was interested in participating in the trial, and where to call. The advertisements and the commercial resulted in an enormous interest to participate in the trial. Around 40,000 people contacted SpinOff during the ten-week period that the commercial was aired and at the time of my observations made up a database where the total number of volunteers is around 80,000 (including volunteers from other recruitment campaigns for other projects). This number of volunteers was more than expected and needed.

This method for finding interested overweight and obese volunteers quickly was thus very efficient, but it was also, to some extent controversial. Some members of the firm's board were worried about how the commercial would be received. Mats feared that a critical discussion about recruitment methods would appear on the cultural pages of daily newspapers, and others feared how colleagues and patients would react. The commercial was therefore tested on some people at the reception of the obesity clinic. Magnus, who was responsible for the Swedish trial, was of the opinion that no one reacted negatively. Not everyone on the board, however, approved of how the commercial was designed, and Mats was afraid it would not be taken seriously. These differing views on the appropriateness of such a commercial can be seen as reflecting the tension inherent in commercialising previously public work tasks.

The television commercial aimed at potential trial participants differs in important ways from the promotional material aimed at the potential clients in the pharmaceutical companies. The main difference is that the television commercial is humoristic and easy for the average overweight man or woman to identify with. It portrays charmingly muddled doctors in white coats running around looking for participants for the trials, a contrast to the serious doctors in the promotional material.

According to Magnus, the medical doctor working in SpinOff and the research department, having the database means a shortening of the patient recruitment process by roughly one year. Out of the 80,000 individuals in SpinOff's database of willing clinical trial participants, 35,280 individuals were selected for screening. They were measured for height, weight, blood pressure and blood sugar level. Out of these, 27,402 patients did not fit the inclusion criteria due to reasons ranging from not having early onset diabetes, having too high or too low blood pressure, or missing other criteria specified by the protocol (see Figure 6.1). Those who did not fit the criteria were excluded. The remaining 4,676 participants were then

checked against the exclusion criteria – also specified in the protocol – and 1,506 were excluded. After further lab evaluations and exclusion of participants who for different reasons decided not to go on, or who were not considered suitable for other reasons, 541 patients remained. These were randomized into treatments with different strengths of the substance or placebo in the study. This extensive selection process from 35,280 to 541 persons took place at 20 different centres in Sweden, and took ten weeks to complete.

Aiding in producing the homogenous group of 541 participants is a computer control system (see Figure 6.2). This control system consists of four different functions. One is a data storage unit for the storing of patient-participant data (A). This database is quite large and consists of data from around 80 000 potential participants. It includes people from across Sweden having either obesity or diabetes, or both. The database is, according to the description at the World International Patent Organization, connected to a “data acquisition means” (B) that aids the nurses or doctors in retrieving data. This is a software that is intended to be used by the research nurse in the trial. In it, she enters the required data for the particular study. A control means (C) is also connected to the storage unit or database (A). This “control means” books appointments or excludes participants on the basis of the data collected earlier through the data acquisition means B and stored in storage unit A. It checks against the database whether the participants have the characteristics required in order to participate in the trial. Finally, connected to this is an appointment booking means (D). This makes it possible to determine when it is no longer necessary to recruit any new participants.

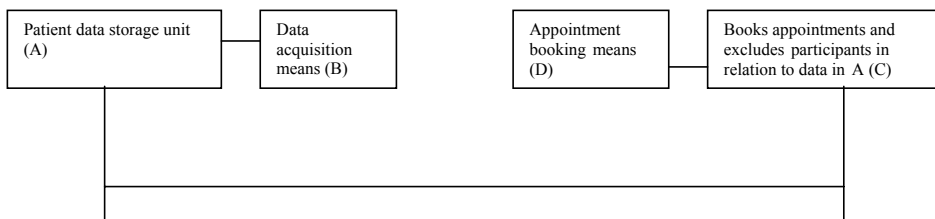


Figure 6.2: The control system used by SpinOff as figured in the World International Patent Organisation (WIPO) application

The research nurse in the Swedish trial can enter data from the participant recruitment process into B, let the system analyse it and include or exclude according to the criteria employed, and finally, on the basis on the result obtained, book the next appointment (or tell the participant that he or she is excluded).

All the information about those who are interested in participating in a study is gathered in one place. The database grows as new participants are added. According to the Swedish legislation on personal data, *personuppgiftslagen* (PUL), SpinOff is legally responsible for the information that it has gathered and stored. The information is used only for medical research and forms a basis for the recruitment of research subjects. When signing up for participation in a study, potential participants agree to have information about their body mass index and what medications they take stored in the database. This is not to be confused with the informed consent form required in every clinical research project that the participant will sign once he or she has passed all inclusion and exclusion criteria. This informed consent form is signed only by the 541 participants who finally enter the study.

The computer system thus serves to coordinate the work of selecting participants in the 20 different centres as well as to coordinate the data gathered in the centres during the trials. It is both a coordinating and controlling tool. The time saved through SpinOff is indisputable. But its implementation was not free from problems in the recruitment phase in the Swedish trial. There were three main issues that arose. First, the system was considered too expensive by the sponsor.⁹ The sponsor has to pay for the screening of 35,280 participant-patients in 20 different centres in Sweden. Usually, this is not something pharmaceutical companies pay for at all, since the traditional way to recruit people is something that doctors do alongside their everyday work without charging anything for it. In the long run, however, and according to Calle and Magnus, the pharmaceutical firm will end up with a better deal since the drug will reach the market sooner

Secondly, and since it was the first time screening had been done in this way, the process involved several practical difficulties for the personnel at the centres. It was not easy to explain to 35,280 minus 541 people that they did not qualify for further participation in the study because they did not have diabetes (or did not fit the other inclusion or exclusion criteria). Also, at one point, the computer system crashed in the middle of a day of screening. This meant that the evaluations needed in (D), saying if a participant was included or not, did

⁹ Interview with PharmaCo's representative, February 2002.

not work. The nurses working with the screening had to rely on pencil and paper during the breakdown, something which put increased pressure on them.

These practical problems had to be dealt with by the staff in the clinics. The ten weeks of screening participants was an intense working period. During this phase, 72 participants per week passed through the obesity clinic with 4 nurses working full time. Finding time to answer different questions that participants brought up was not sufficiently planned for within the time frame provided by the system. The system's developers are aware of the problems caused by the intense scheduling. Calle, the head of software design, admits that they "crossed the limits" in certain situations.

And it probably wasn't formally a technical question but the project outline itself... and the time frames we were given as input. Which takes us there again – that the technology and the system is only a tool, and that what one feeds into it is what it will try to follow through and try to operate. If one says that there are three weeks between the visits, then there will be. So it is not so much a technical problem, more that we really pushed the limits too hard. There was not enough room to make mistakes.

(Calle)

A third problem that arose in the middle of the screening process was that the number of participants was too low. Some people that had been enrolled never showed up and others did not fit the specified criteria. More people had to be screened and new participants added. These extra participants were all screened at the obesity centre since it turned out to be easier to find participants in that specific geographic region. This led to a somewhat chaotic situation for the nurses and other staff in the clinic at Centre University Hospital and a very intense work load for the research nurse in charge of the Swedish trial, as well as for the other nurses and dieticians involved.

Scheduling clinical trial work

After the 541 participants had been selected and recruited, SpinOff controlled the scheduling of their appointments throughout their participation in the trial. For the scientific quality of the study it is crucial that the participants at the 20 different centres are tested in the same way and at all the visits specified in the protocol (see chapter seven). This means that the time period between appointments should be the same for all participants, and in all centres. If and when a participant cannot make an appointment, it is important to reschedule him or her in a

way that fits the availability of staff and confirms the time frames specified in the protocol. Aiding the nurse in this scheduling is the computer system's appointment booking (D in Figure 6.2).

The computer system's management of the scheduling has certain similarities to an industrial production process. The patients, metaphorically of course, become the "raw material" that is processed in order to produce the data. This is evident in how the clinical trial is talked about in industrial production line metaphors, as in the following excerpt. Here, software developer Calle talks about how he thinks about the computer system:

...much of the thought model behind it is that this is really a conveyor belt. There are certain processing stations on the way, and then there is a raw material that you put in somewhere, which then relates to these processing stations. They haven't been in them yet, or they're going there, and they may still be out in the storage room. But it is a certain procedure that is to be described, and you're to identify them in all places and know what has happened to them. It's exactly the same model you have when you run a factory.

[...]

Yes, and the program's name is "The Factory" when you start it there... and they have machines that do every examination in a machine. And you have selectors... they are the ones that run out in the storage and get the patients that are ready to... "now they will be painted, they were polished in the previous step"... so give me all the polished ones in rack eight... And then the truck goes away and gets them, and then they're out. We don't want to talk much about this but it's a good model to think with. It makes it very easy for many people to think in these... It's a concrete model that you can gather around, both medicine people and technicians and discuss where you are and what the next step is and so on.

Their remark shows that factory production was seen as a model for the management of the clinical trial. To depict what goes on in the trial, factory metaphors were used referring to trucks, racks, conveyor belts, raw material and selectors, not to mention the term factory itself. The thought model behind the computer system sees the clinical trial process as a virtual conveyor belt, with a number of processing stations, such as an echocardiogram to be taken, or a blood pressure to be measured. The number of processing stations were many which is why keeping track of where the raw material is in the process was important.

The question is whether these metaphors are adequate to describe what goes on in a clinical trial. When does a metaphor stop being a metaphor and turn into being something? Is

the randomised controlled drug trial, or parts of it, in fact the same thing as production in a factory? From Calle's perspective it seems like any other production process. In his words:

You could think about how much [of it] is university research and how much is really some other kind of activity. You do build on a lot of other know-how, not related to research. It is about knowledge on logistics... project leadership... a lot of things that are needed for carrying on research activities.

(Calle)

His views on the clinical drug trials focus on the nitty gritty work of dealing with large scale projects in terms of recruitment of patients and other logistics.

If you contemplate this a bit coldly... this isn't big and beautiful science where heroic people in a cloak stand on mountain tops and point in the direction towards the descending sun, or something like that... It's a craftsmanship that is to be done, and what you're striving for is a proof of whether this works or not.

Thus, in his view, conducting clinical trials are a mixture of production and craft-like management rather than "pure" science. The complex organisation and the great number of people and tools needed to conduct trials such as the Obe ones, make the activities into a complex web of research, logistics and project leadership.

The computer control system is a tool used to keep track of where in the production chain the participants are at a specific point in time. If production proceeds smoothly, the conveyor belt rolls on without interruptions; the trial staff, or metaphorical trucks that transport the participants to the right stations, see to it that the participants and all necessary equipment are in the right place at the right time. Personnel follow what the computer system tells them to do. In a sense, the computer system controls what they do.

Standardization implies a control of different actors to conform to a standard in order for coordination and uniformity of work to be done. This control, however, as Timmermans and Leiter have pointed out, occurs at the expense of individual autonomy and responsibility. Thus, every standardization system implies a "precarious balancing act between control and flexibility" (Timmermans and Leiter 2000: 42). A degree of flexibility and autonomy for the workers is necessary to keep them enrolled, but could entail the risk that prescribed tasks are modified or bypassed. Too much control means actors may be unwilling to follow the prescribed tasks. When Calle talks about the computer control system, which can be seen as a

standardization system making the work process proceed more efficiently, this balancing act becomes evident. He here describes the way he sees the role of the computer control system:

...it's a combination of control and still some form of flexibility [...] Staff can solve problems much better themselves than we ever could do... on a small local level.

He then gives an example of how there has to be flexibility built in the system in order for the job to be done:

If for example [we] have made an original plan to meet a certain amount of patients and do certain things in a certain time, and then it turns out that it isn't possible...that it takes too long from the point when we have taken a lab test to when we get the results... [then] our plan from the start was that we could have one and a half weeks between the visits [scheduled in the system], which is what the protocol prescribes. So that's why we've put in one and a half weeks. Then it turns out that we have to put in two weeks since we haven't gotten the lab results... without which we cannot make a decision [whether or not the patient's tests results allow him or her to stay on in the study]...then it's the staff at the centres that are excellent in handling it. And our system must be capable of collecting information from them about changing the schedule.

The system needs to be flexible enough to take in information even if it arrives later than the system had prescribed. The job of handling the kind of information brought from an unanticipated event such as the late arrival of lab results is best done by staff at each centre.

This chapter has focussed on two ways in which SpinOff's computer control system makes clinical trial work more efficient. The first way SpinOff functions in the Swedish Obe trial is to shorten the time involved in recruiting participants. The second way is to make clinical trial process "flow" more smoothly, both in terms time won in testing and as well as control of when the tasks were performed.

I have showed how this is done by tools developed in industrial production processes, and made applicable in clinical trials. From this it becomes evident that a clinical trial process can be controlled in the same manner as any other kind of production. What the tool enables, is the quick recruitment of a homogenous group of participants. This is what SpinOff has been most successful in doing. The implied shortening of the total time a clinical trial takes to perform is well needed by pharmaceutical companies who try to cut costs in any way

possible. Following from this, the process of selecting suitable participants to a clinical trial can be said to have been not only commercialized, in the sense that previously public funded tasks have become part of a private firm's activities, but also as part of a wider effort to rationalize the production process in order for it to become more predictable and smooth.

Before SpinOff was started, these rationalization efforts were made within the hospital. The difference that is made by commercializing the work tasks is that such commercialization enables using tools and staff from the private industry, and thus opening for competition with other private companies. The work process that has been rationalized by SpinOff is also rationalized by another central tool in randomized controlled trials: the clinical research protocol. It is to this tool that I turn in the next chapter.

Rationalizing tools II:

The clinical research protocol

Understanding medical practices is difficult without taking into account the different types of written documents used such as rules, guidelines, medical journals and protocols. The most pervasive document in a clinical trial is the clinical research protocol. Protocols appear frequently in medical practices and, according to Marc Berg, can be seen as a set of standardized instructions helping staff at a clinic to know what to do at a particular point in time. Such instructions can be more or less detailed, elaborate or binding and can have different appearances and structures. They can consist of very general recommendations or can be in the shape of a very precise chart showing nearly exactly what to do in a certain situation. What different protocols have in common is that they all guide staff through a sequence of steps (Berg 1997: 52). In clinical drug trials the protocol is an extensive document which in great detail describes all the tests that are to be taken, in what order and, often, according to which standards,

A protocol also “functions as a focal point of reference – a common resource – to which various staff members refer, can orient themselves and can find clues on what to do next” (Berg 1997: 138). The ways in which clinical trials are performed have become increasingly standardized, as the following descriptions of the protocol used in the Obe trial, will make evident. Complex and large-scale projects cannot do without such standards (Star & Bowker 1999: 13 ff.) The standards serve an important function in that they make things work in as similar a way as possible across distances. Thus, standards both make complex projects possible, but they are problematic in that they, by definition, do not fit every practice and every person they are designed to work for. Therefore, and as Star has pointed out, to those who they may not necessarily be standardized for, standards can become problematic (Star 1991a).

The purpose in this chapter is to describe the clinical research protocols used in the Swedish trial. It will give a sense of what the patient-participant trajectory through the trial would be if followed through in the ideal way prescribed by the protocol. That this trajectory

often is not so smooth and ideal is something that the different staff groups are very well aware of. The contingencies of practice make the protocol indispensable when a large-scale and multi-sited project such as the Swedish trial is to be conducted. It lessens contingency. In focus in this chapter is the protocol as a coordinating device necessary for conducting multi-sited and extensive production of data, while chapters eight and nine, will deal with the everyday practices of trial work and how the protocol fits into these.

Contents of the Swedish trial's protocol

Obesity researchers call obesity a "multi factor disease", which means that there are many different explanations as to why some people gain so much weight. Medical explanations range from defects in appetite regulation to body energy balance (Astrup 1998). There is no scientific evidence of overweight people having "low metabolism", which is commonly assumed. Low energy expenditure does not lead to obesity; there are many other variables that contribute to gain weight (Goran 2000).

Medical research in Sweden has shown a significant increase of obesity since 1980/1981, with the greatest change measured between 1988 and 1997 (Lissner et al. 2000: 804). At the same time, diabetes has also been declared a global epidemic, with a measured increase in prevalence of 33 per cent in the USA between 1990 and 1998.¹⁰ Obesity and low levels of physical activity are said to play a large part in this increase. This was one reason behind studying the effect of Obe on type 2 diabetes. According to Wing (2000), as much as 80-90 per cent of people with type 2 diabetes are obese. Obesity has also been shown to worsen metabolic and physiologic "abnormalities" associated with diabetes, such as hyperglycemia, hyperlipidemia and hypertension (Maggio 1997).

The close relationship between type 2 diabetes and obesity implies that diabetes must be taken into account in clinical trials on drugs against obesity. In the Swedish trial, the effect of Obe on type 2 diabetes is the primary research question, while its effect on obesity is the primary question in the international trial. The character of the relationship between obesity and diabetes is debated. Swedish researcher Mats Eliasson (2002) means that the risk of getting diabetes is related to abdominal obesity rather than to the total amount of body fat. The proportion of type 2 diabetics has not increased at the same pace as the proportion of persons with BMI over 30 (World Health Organization's MONICA report 1987), indicating

¹⁰ According to the American epidemics authority CDC, Centers for Disease Control and Prevention

that it is possible to debate a straight relationship, or even causality, between the development of type 2 diabetes and weight gain.

Weight loss for people with diabetes has also been shown to improve low density lipoprotein cholesterol levels, lipid profiles, as well as mental health and quality of life. However, these improvements are only meaningful if weight loss is sustained over time (Wing 1985), and there are no treatments, aside surgery, that have been shown to result in sustained weight loss on a long term basis. The weight lost, it seems, is always regained and the patients regain their previous weight after successful interventions. The drugs that have been tested do not provide a long term weight loss, and seldom even produce significantly large weight loss. The testing of Obe therefore also has to focus on the effects that can be measured in other risk areas such as cardiovascular disease, the metabolic risk profile and quality of life. These different biomedical aspects of obesity are all part of the background to why the trial is designed in a specific way. It also explains part of the reason to why the trials involve such a high number of testing procedures.

The work of each individual drug trial in the basement of the clinic is largely structured by the clinical protocol. In the Swedish trial, it is a lengthy document consisting of eighty-five pages, size A4. In it, most of the information needed for the conducting and following through of the trial is presented. It explains the objectives of the study (to assess the efficacy and safety of Obe), and gives a detailed description of the study's design, as well as information about the study population.

For a social scientist or someone not familiar with clinical trials, reading through the protocol opens up a whole new world of concepts. The pharmaceutical firm is termed the "Sponsor" with a capital S. The person in charge of the drug study at the clinic is referred to as the "Investigator" with at capital I. The study participants are referred to as "subjects" (no capital s). It is written in English, in a dry medical scientific prose and peppered with minute medical details that are often difficult for a lay person to understand.

It is not clear who is behind the protocol in terms of authorship, except for some information on the second page. Here, there are two signatures from a "Co-Chairman, Clinical" and a "Co-Chairman, Statistics" who constitute the "protocol review committee". Below these is the signature of the "Global Product Leader". The instructions in the protocol are formulated in the future tense and passive form (i.e. "weight will be measured for enrollment assessment..."), something that adds to the sense of a formal and somewhat dictatorial text.

The intended reader of the protocol is not clear. Even though the “Investigator” is to sign a paper agreeing, among other things, that the protocol “contains all necessary details for carrying out this study” (p. 11), the information supplied may not be understandable for all staff groups. It contains information on pre-clinical studies of the substance that may be difficult to interpret, even for the trained medical doctor. Moreover, the information is not necessarily useful to all its readers. The nurses said that they had read the protocol, but all information was not meaningful for them:

I really haven't read the whole protocol to be honest. But you use it a bit like an encyclopaedia where you can look up how you are supposed to do something.

(Nina)

Throughout the text are references to other documents. For instance, where details about toxicology and pharmacokinetic profile of the drug is given, the reader is referred to the “Investigator’s Brochure”, where even more detailed information is given. This information however, is only available to the Investigator and not to the clinical trial staff, should they have the interest or need, if unlikely, to look up such details. When it comes to different measuring practices, the protocol refers to standard diagnostic criteria for how diabetes is measured, something which here implies following the American Diabetes Association’s Clinical Practice Recommendations from 2000. The protocol also refers to heart functioning classification standards that, similarly, follow standard criteria, in this case the New York Heart Association Functional Classification. Finally, there are references to rules and regulations concerning clinical trials and medical practice, where the most often mentioned are the Helsinki Declaration and GCP standard (Good Clinical Practice). These and other examples give a picture of the protocol as a system of standards and classifications.

The rules and guidelines around how clinical trials should proceed have become stricter and more bountiful in later years. Guidelines for clinical trials were first formed by the American Food and Drug Administration, FDA. In England it was the pharmaceutical industry itself that formulated the first guidelines and in France it was the Ministry of Health that produced guidelines, which later became law. Presently there is a great amount of work being done to go through these different kinds of guidelines and make them into global directives. This work means a harmonising of American, European and Japanese rules and guidelines through a large international forum – International Conference of Harmonization

(ICH). In specific cases this process has gone well and come quite a way. Good Clinical Practice (GCP) is one example of the results of harmonization and it is allegedly being followed in all clinical trials. GCP has two goals: to protect the interests of participating patients and to ensure that clinical research is being done in a highly qualitative and correct way, as well as in a manner that can be controlled post-trial (Lemne 1991/1997: 13). The pharmaceutical companies design their own internal standard operating procedures, SOP's. These are supposed to be in line with the GCP.

In the protocol, these standard rules and guidelines are being incorporated. When questions related to medical ethics in clinical trials are tried by local or regional ethical committees, the protocol is an important source on which committees base their recommendations and judgements.

The scale of the trials and the increasing complexity of global standards for clinical research as represented by the clinical research protocol also make for another problem. The dense information in a protocol makes it difficult for lay people to influence or critique the protocol. When receiving critique for having high costs in production, pharmaceutical companies can refer to rigorous safety and quality standards. But, as Barry has pointed out, such standards are not only about ensuring safe and high quality trials. They may also be beneficial to the companies in that it helps them defend themselves against cheaper competition (Barry 2001: 51), and serve, in practice, "as a means of competition between firms" (Jacobsson 1998: 144). Standards, further, create problems such as depoliticization, technification and unaccountable regulation (Jacobsson 1998: 146, Barry 2001: 205). Another problem with standards is the problem of accountability. Knowledge is stored in the standard, not in the person. Accountability is distributed.

One of the doctors in my study, Mats, also talked about the increasing levels of bureaucracy, following increasing complexity in clinical trial design. In the following, when referring to a meeting he attended at the Medical Products Agency, he indicates how he thinks that the increasing levels of bureaucracy are not only about protecting the individual participant-patient:

Officially, it has to do with patient protection... or, rather consumer [protection]. The question is if they [the MPA] didn't think that all the paperwork and formalia that is needed [in medical research] is at the risk of suffocating all independent research. And this, I think they realized but "that's the price we have to pay", they seemed to think. And that's something to think about. But you do, principally, need experts in judicial

issues concerning trials and all the formalities, Good Clinical Practice, etc. on a paper level in order to keep a project on the road... Plus the financing.

(Mats)

The protocol can be seen as the script on which trial practice is based. It therefore also contains certain assumptions about the work situation at hand. Berg mentions three assumptions inherent in protocols concerning medical data, medical criteria and medical work. The first is that there is an underlying view that

[...]the *medical data* are well-defined sets of clear-cut, elementary bits of information which are to be uncovered by looking, asking or performing a test. In addition, they assume that *medical criteria* are similarly well-defined and pre-set: they are depicted as fixed rules that merely have to be 'applied'. When situation Y is present, then X should be done. Finally they depict medical work as a *sequence of circumscribed, individual steps*, each of which needs to be terminated before the following can be made.

(Berg 1996: 119, italics in original).

These assumptions inherent in the protocol imply an ideal-typical and universal sounding image of how "a situation" is to be judged. This underlying view in a protocol reduces a complex reality into one that is predictable and open for intervention, something which is both its strength and weakness. Without it, a clinical trial (especially a multi-centre one) could not be performed in such a similar way at many different places at the same time. On the other hand, it makes invisible part of the work that is done in order for it to work in everyday practice, something I will return to in chapter nine. To analytically separate the tasks specified in the protocol from the ones that are made invisible by it, I use the distinction between production tasks and articulation work (Fujimura 1987: 258), where production tasks refer to tasks which are "relatively well-defined", in contrast to tasks performed around the protocol in order to coordinate production tasks and to make the job doable: articulation work. Articulation work is, by definition, not mentioned in the protocol. The inherent view in the protocol, following this distinction and Berg's description above, is that medical work as represented by a protocol is a set of production tasks. In the rest of this chapter I will describe what these production tasks are, as outlined in the protocol, while the following two chapters also analyse the articulation work necessary to make the protocol work.

Production tasks in the protocol

The protocol includes a summary of when all the different production tasks are to take place during the 66 week trial period. This is called the “time and event schedule” (see Figure 7.1), and is frequently consulted by the research nurses. It summarizes what specific tasks are to be done at what time. The time and event schedule has been reproduced on a thicker piece of paper and has been plastic-coated, enabling frequent use.

The trial consists of four different phases: a run-in phase, a titration phase where the dosage is increased step-by-step, a maintenance phase, and a follow-up phase. It is in the pre-enrolment and run-in phases that SpinOff is most involved, since this is where the 541 participants or, in protocol terms, “study population” are selected. Visits 1 to Visit 5 are part of this selection process (see Figure 7.1). Those participants who are not excluded they go on to Visit 6, which in this protocol is where the “baseline” is located. Baseline is where the study really starts in terms of producing extensive amounts of participant data for the pharmaceutical firm. This is where the participant signs the informed consent form.

Inclusion and exclusion criteria

The first thing that the staff has to decide upon, according to the protocol, it is whether the participant is suitable for the study or not. This is done by the staff applying a number of inclusion and exclusion criteria specified in the protocol. To fit into the study, participants need to meet or not meet with the inclusion and exclusion criteria. Inclusion criteria in clinical trials are usually relatively few and give a general description of the ideal research subject according to a pre-set norm. The wide inclusion criteria for the Swedish trial are 1) being between 18 and 75 years old; 2) having a body mass index (BMI) of 27 or more, and; 3) having an early onset of type 2 diabetes. The exclusion criteria, on the other hand, describe all the exceptions from the rule and are thus more narrow. Some of these criteria are included in order to avoid risks already known from previous studies, other are there to control that certain specified factors such as weight levels, hypertension, medication levels, and smoking or alcohol levels are relatively stable.

Figure 7.1: the Swedish trial protocol's Time and Event Schedule

Phase of Study	Pre-Enrollment		Run-In Phase				Titration Phase			
	Pre-Enrollment 1	Pre-Enrollment 2	Enrollment			Baseline ^c				
Visit	1	2	3a	3b	4	5	6 ^c	7	8	9
Procedure / Week ^{II}	-12	-11	-7	-6	-4	-2	0	2	4	6
Informed Consent ^b	X	X								
Advert questionnaire	X ^A									
Medical History		X		X						
Height	X ^A		X							
Entry Criteria	X ^A	X	X	X			X			
BMI	X ^A		X	X			X	X	X	X
TSH, Drug Screen			X							
FSH			X							
Routine Study Visit										
Call IVRS & Dispense meds. with diaries				X			X	X	X	X
Drug Accountability					X	X	X	X	X	X
Non-pharmacologic Therapy ^k				X	X	X	X	X	X	X
Adverse Events & Conc. Medication					X	X	X	X	X	X
BP ^f , Pulse & Weight	X ^A		X ^A	X	X	X	X	X	X	X
Urine Pregnancy Test			X		X		X		X	
Waist/Hip Measurement			X				X			
Sagittal Diameter, Neck Circumference			X				X			
Physical Examination		X		X			X			
12-lead ECG			X				X			
Blood Chemistry, Hematology, Urinalysis			X				X			
OGTT, Clotting factors, Fasting Insulin, C peptide & Urine Albumin			X ^A	X			X			
Lipid Profile			X				X			
HbA _{1c} & FPG	X ^A		X				X		X	
Plasma [REDACTED]										X
HRQOL ^g			X				X			
GRC										
Recalculate caloric content of diet										
For selected sites the following will be completed										
Echocardiogram			X				X			
Renal ultrasound			X				X			
Body composition; DEXA and CT scan				X			X			
Ophthalmologic and visual assessments ^l							X			

se	Maintenance Phase													Discontinuation Phase		
10	11	12	13	14	15	16	17	18	19	20	21	22	23 ^b	24	25	
8	12	16	20	24	28	32	36	40	44	48	52	56	60	62	66	
X	X	X	X	X	X	X	X	X	X	X	X	X	X			

X	X	X	X	X	X	X	X	X	X	X	X	X	X		
X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
						X							X	X	
						X							X	X	
						X							X	X	X
						X							X	X	
						X							X	X	
						X							X	X	
X	X	X	X	X	X	X	X	X	X	X	X	X	X		X
						X							X		
X			X			X							X		
						X							X		

						X							X		
						X							X		
						X							X		
						X							X		

The exclusion criteria are not all explicit in the protocol. For example, number 28 on the exclusion criteria list opens up for a participant to be excluded if there is some other condition that the investigator fears will be a problem for participation. Such a reason could be the doctor not considering the participant suited for partaking, due to not being motivated enough, or based on a belief that the participant has not fully understood what is required from him or her. Therefore, it is crucial for the investigator to establish a rapport with the participant if the participant is to be allowed to continue in the study. The corresponding term used in medical research to establish rapport is “compliance”, where participants not likely to stay compliant to the protocol are excluded. How personnel work to make participants compliant is discussed further in chapter nine. An underlying but not explicit purpose of the pre-enrollment phase is also to weed out participants on the grounds that they did not turn up according to schedule (cf Oudshoorn 2003: 176)

The purpose of the exclusion criteria is also to avoid having already known risk groups such as pregnant or breast-feeding women (where babies and foetuses must be protected). Participants that, from earlier trials on Obe, are known to be at risk of other well-known side effects are also excluded from participating in the trial. Thus, participants having a family history of kidney stones, eye problems such as glaucoma or cataracts are excluded. The exclusion criteria are also, and perhaps less self-evident, used for the purpose of having a more homogenous study population with as few “confounding factors” as possible, that is factors that can affect or disrupt the result in any way (Lemne 1991/1997: 29). There are benefits to having narrow as well as having wide criteria in a clinical trial. Having few exclusion criteria makes it easier to find research subjects within a reasonable time period. The problem with such wide criteria, however, is that the study population becomes less homogenous which will lead to less unequivocal research results. On the other hand, it will create more generalizable results (Ibid.). The group of patients finally enrolled in the trial discussed here is thus a relatively homogenous one.

The process whereby participants are selected to participate in a clinical trial can be compared to that of the groups who participated in the clinical trials of AIDS medication where the participants were white middle-class men without drug problems (Epstein 1996). Epstein shows how these patients were seen as ideal patients for the health care system, as well as for the pharmaceutical industry since they were considered likely, due to their stable life situation, to stay compliant to the protocol requirements and be unlikely to drop out.

From reading the inclusion criteria it becomes apparent that stable and low risk participants are wanted for the trials. The protocol asks for participants who have “the established co-morbidities”, such as type 2 diabetes, hypertension or dyslipidemia. What is tested, in the later stages of the trial, is not only weight loss but also how the substance affects blood pressure, blood sugar and cholesterol levels in participants already exhibiting (low) risk levels of each problematic condition. It also asks for participants who are stable enough in their weight so that they are easily comparable against each other.

The formulation of inclusion and exclusion criteria has been likened to “configuring the user” by Van Kammen (2000). The eventual future user, however, does not necessarily have the same narrow characteristics as the participants who were included in the trial. Having narrow criteria, therefore, make for a narrow and homogenous group of trial participants that may not reflect the diverse characteristics of the large group of intended users.

In order to ensure that the participants continue to live up to the entry criteria, and in order to make it less likely that they will drop out, criteria are reviewed five times including the last time at “baseline” in visit 6. The number of participants who finally are randomised to a treatment at baseline is, as has been pointed out earlier in chapter six, relatively small compared to the amount of participants at the pre-enrollment visits 1 and 2. The five visits preceding baseline are designed to make sure that the test results at baseline do not come as a total surprise, creating the need for a redesign of the study. Study designers need to know that the group of people randomised at baseline will be likely to both continue to meet the entry criteria throughout the study, as well as that they have proven to be compliant and are judged likely to remain so throughout the study.

In the Swedish trial it is difficult to enrol people because they are not aware that they can be classified as having diabetes type 2 and therefore have not previously been in contact with the hospital. The 35,280 people screened in order to find participants with “previously undiagnosed diabetes”, are what the monitor of PharmaCo terms *indikationsnaiva*, or naïve of their indication. Thus, finding persons who have an indication that they are not aware of requires special recruitment methods other than in a situation where patients know they have the condition required.

The second visit that the calculated 4,676 participants attend is done one week after the first visit. Here, information about participation in the drug study, and not just the pre-enrolment phase, is given and participants are allowed time to ask questions concerning the study, and granted additional time to consider her or his participation. Once the participant has agreed, the informed consent paper is to be signed. The participants also go through a

physical examination and are checked to see if they still are eligible for the study, in line with the inclusion and exclusion criteria. This visit can be seen as a way of preparing the group of participants for the next phase, the enrolment phase, since the tests that are taken are both time consuming and sometimes expensive for the sponsor in terms of the use of advanced equipment.

During the six week enrollment phase (visit 3a and 3b), the participants are started on the weight reduction therapy provided by a dietician. This is also where the participants start taking the drug under study. Through the run-in phase that starts with the enrollment visits and ends with the baseline visit, participants who experience problems with using the drug or in other ways are not “compliant” can be excluded before baseline, making it possible to have better throughput, or flow, of participants in the study. The participants who reach baseline are more likely to stay “compliant” throughout the whole of the trial, thereby lessening the risk of many drop-outs.

The subsequent 19 visits are to take place within a 66 week period. All activities are precisely scheduled, as are the precise details on how the nurses, doctors and dieticians are to proceed. After the participants have passed through the inclusion/exclusion criteria and agreed to become enrolled in the study, they go through a number of stations in the time and event schedule. The participant agrees to participation through signing a form of informed consent. Thereby, the participant is seen to be aware of the implications of being part of the study and also aware of the risks involved. These risks are the already known side effects such as dizziness and mood swings. After the enrolment visits, the participants are randomised into four different groups given, respectively, three different doses of the substance or a placebo.

Production tasks at the stations

Many different tests and measurements are scheduled for each of the 25 visits. The clinical protocol attempts to give all the details needed for the nurses, doctors and dieticians to carry out the study and “collect” the data or produce the inscriptions. To be able to measure the efficacy of the substance many assessments are made. Body weight, body mass index (BMI), anthropometric assessments, glucose tolerance, lipid profile, insulin response to glucose, blood pressure, quality of life, and body composition are assessed in the different visits. Anthropometric assessments include hip and waist measurements as well as the ratio of hip and waist (WHR). The hip waist ratio indicates the risk of being in the risk zone for diseases of the heart and arteries. These diseases are related to belly fat rather than the total amount of

fat in the body, which is what is measured with BMI. In order to be able to judge the risks of obesity a combination of the methods BMI and WHR are used.

Also, detailed instructions are given in the protocol as to how participants are to be dressed when having their height, weight and waist-hip relation measured. This, again, is in order for the measurements to be done in the same way in the different sites:

Height will be measured using a wall-mounted stadiometer or one mounted on a balance beam scale, whichever is most appropriate for the individual subject. Subjects should be barefoot or wearing socks and must not be wearing shoes.

Weight will be measured (for this and subsequent visits) using a standardized calibrated balance. Subjects will wear light clothing (i.e., no jackets, sweaters, or shoes). Subjects will be weighed in similar attire at each visit and at approximately the same time of the day. The standardized calibrated balance should be calibrated every three months and calibration documented.

Waist and hip circumference measurements (for this and all subsequent visits) will be taken with the subject standing, wearing underwear, with or without a gown. The waist measurement will be performed at a level midway between the superior aspect of the iliac crests and the lower lateral margin of the ribs. The measurement need not be at the level of the umbilicus. Hip circumference will be performed at the level of the pubic symphysis anteriorly and the greater femoral trochanters laterally. The measuring tape will be kept horizontal for both measurements. Attachment 5 provides a diagrammatic explanation.

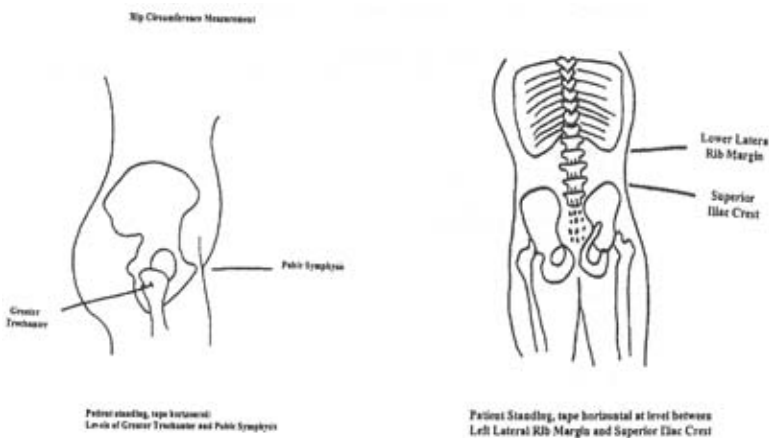


Figure 7.2 Anthropometric measurements

The way in which to measure blood pressure is likewise minutely described:

Blood pressure will be measured (for this and subsequent visits) in the same arm throughout the study, using a wall-mounted mercury sphygmomanometer. Three consecutive measurements will be taken at each visit and recorded. Blood pressure will be taken after the subject has been sitting resting quietly for five minutes. The investigator is encouraged to use the same appropriately sized arm cuff throughout the study. Cuff size and subsequent changes to cuff size should be recorded in the subject notes.

For the testing of blood sugar levels, the oral glucose tolerance test (OGTT), participants are required to have been on a minimum eight hour fast before showing up at the hospital. The OGTT is done according to a standard OGTT procedural manual attached to the protocol. The OGTT measures how the body reacts to intakes of sugar. There are two blood extractions performed. The blood samples taken from the first extraction are used for analysing very large amounts of standard clinical laboratory assessments (blood chemistries, haematology, etc.). In the second blood is drawn after the patient has been given an orange coloured sugary liquid, allegedly tasting like orange soda but not carbonated.

After the liquid in the OGTT has been administered to the participant, he or she is, according to the protocol, to be given the equally standard questionnaire called Health-related Quality of Life Measures, (HRQOL). It is clear that being overweight many times affect people in negative ways not measurable by medical tests, such as those described above. The psychological well-being of the participants is therefore also measured in the international trial and the Swedish trial. This is done through yet another standardized form, the Quality of Life questionnaire, the HRQOL.

Even the way the HRQOL questionnaire is to be delivered and answered is specified in the protocol:

Subject must complete questionnaires in a quiet, semi-private area, after blood has been drawn for the OGTT and the solution has been administered and prior to any clinical assessments; administration of any efficacy measures or to seeing the physician.

This and other citations are examples of what Berg has referred to as the fixed rules that are simply ready to be applied to practice, inherent in the protocol. The HRQOL is then being

administered on visits 3a11, 6, 10, 13, 16 and 23, so that it will be possible to follow up on “changes in life quality” during the whole trial period.

Urine analysis is also required, in order to measure urine albumin and conduct urine drug screening and a urine pregnancy test in the case of fertile women. A general physical examination is also to be done, where the participant sees a doctor and talks about individual health issues or problems. The forms these physical examinations should take are one of the few things not specified in the protocol. The issues to be brought up in these meetings are up to the individual participant or trial doctor to decide upon. Here, the protocol is quite open and says it is up to the clinical judgement of the doctor who is taking care of the visit. The doctor’s visits consist of a physical examination, where the doctor checks if the participant is of good health as well as if they still fit the inclusion criteria specified in the protocol.

Another procedure part of the protocol is an echocardiogram. This 12-lead ECG is recorded with the patient lying down, and is then sent via a telephone to a CRO (contract research organization) firm in the United States. After about ten minutes the result comes back to the clinic by fax.

The distribution of fat in the body is not only measured through body mass index and waist hip ratio, as described earlier. There are two high-tech measuring devices located upstairs in the clinic, a CT-scan and a DEXA scan. Two nurses work in a pair with the CT scan. The participant lies down and is strapped on to a stretcher that is pushed into the hole in the middle of the machine. Five scans are made of five parts of the body. The visualisations made of the inside of the body make it possible to see how much of the body fat is located inside and outside the abdomen, called visceral and subcutant body fat, respectively. Generally, women are said to have the fat subcutant, while men collect their body fat inside the abdomen; hence the image of men with big bellies and women with big backs and thighs. From the CT scan, it is also possible to see how small or big the internal organs are and thereby estimate their weight. This is needed in order to estimate the total amount of body fat.

After the procedure around the CT, it is time for measurements by DEXA. Here, how much of the body weight consists of bone mass is measured. The DEXA is a very low-radiation machine that gives a visual representation of how much of the body consists of bones. The study participant has to lie down once again and be strapped to the machine. This procedure is not as quick as the CT; the arm moving on top of the strapped patient moves very

¹¹ Visit 3, or the enrollment visit is divided into two parts. This is done in order to “allow the review of laboratory parameters essential in the assessment of entry requirements” (protocol p. 32).

slowly. The strapping, and thus immobilization of the participant is important for the quality of the pictures taken. As the arm of the DEXA moves, an image of the body skeleton appears on a screen attended by a nurse. The whole procedure takes around twenty minutes.

Finally, after going through all this measuring and weighing, the participant is to meet a dietician to discuss the different ways to lose weight and start exercising. The dietary treatment consists of one standardized and one individual part. The standardized program is called “Pathways to Change” and is designed to help the participants in making the changes in lifestyle needed if they are to lose weight. Again, it is important to use the same program in all locations so that the whole trial is conducted as homogeneously as possible. Every visit (or “lesson”) with the dietician is numbered and is to focus on the same subjects in all trial sites at the same time. The titles of the four lessons are: 1) *Why Lose Weight?* 2) *The Change Process: How, When and What to Do*, 3) *Positive Thinking for Weight Control*, and finally 4) *Now That It’s Off, Keep it Off!* These standardized lessons originate from North America.

The vast amount of data gathered through following the protocol are collected and marked in a standardized form, the case report form (CRF). In the case of the international trial, a CRF consists of one five decimetre thick, binded file per patient which is stored in a locked cupboard. The most important instructions of the protocol are repeated in the CRF, which makes the tasks easier to perform than if the protocol had to be consulted on a daily basis. Once the study is on its way, these forms are used on an everyday basis together with the time and event schedule (Figure 7.1).

The CRF is designed in a way that makes the data easy to process by computer. It is very important that all the data is correct. To control that data entry is done properly, the pharmaceutical firm sponsor sends a monitor to the clinic on a regular basis. It can be difficult to distinguish between symptoms that are caused by the administered substance and symptoms caused by the patient’s life situation in general, or decide if the symptoms are a result of a combination of the two. This demands that both nurses and doctor will have to consider whether to report side effects to the CRF or not. The reporting is not only done in the CRF, but in a patient journal as well. This double reporting is done to make it possible for the clinic to follow up on the health related issues of the trial later, since the information entered into the CRF belongs to PharmaCo. In the event of something happening to the participant, a medical journal has to be kept as well. The material entered into the CRF can therefore be said to be concerned with *study related* issues and with those involved as *participants*, whereas the medical journal has to do with the health of the *patients*.

Protocol amendments

So far, the protocol has been described as a very stable and standardized document used to collect ideal-type universal information. But real practice is never so smooth as the standard prescribes. Changes in practice have effects on the protocol. In the Swedish trial, seven amendments were made to the protocol throughout the course of the trial. The most important amendments were made as a direct result of the unexpected side effects that occurred. Three changes were made by the monitoring board. One was increased monitoring of blood chemistry by adding tests to the remaining visits. The second was an extra safety measure in the shape of an alarm system to control liver enzyme levels of the participants. The central laboratory was directed to alarm the principal investigator and the monitor through fax and telephone if the enzyme levels (ASAT and/or ALAT) rise to three times the upper normal level, so that a decision can be made as to whether to exclude the participant from further participation or not. The third measure taken was to evaluate the liver function tests non-blinded and to involve independent liver experts in the specific cases where side effects have occurred. Following these changes, the participants needed to sign a new informed consent form where this new information was added.

Thus, events such as unexpected side effects led to changes in the protocol during the course of the trial, which shows that the protocol is not irrefutable, but can be changed if an unexpected situation requires it. As I will discuss, using a protocol is also not only a question of applying instructions to practice, as it may seem from only looking at the design of the tools. When the protocol was localized by the nurses, doctors and dieticians in the basement where the Obe trials were performed, different kinds of less visible tasks were needed. This kind of work will be the focus in the following chapters.

Producing reliable data

The clinical research protocol gives detailed instructions, serves as a coordinating tool, and enables the clinical trial process to be performed simultaneously in 20 (in the Swedish trial) or 40 sites (in the international trial). Personnel in the clinic perform a multitude of practices in order for the process to proceed smoothly. In the Swedish trial, the management of the work processes is also done with the help of a computer control system. This and the following two chapters look at how these tools operate on the floor from the perspective of the tools' users: nurses, dieticians and doctors. This chapter examines how the protocol is made into a useful tool in order to produce reliable data, bearing in mind that the trials are large scale, multi-sited and involve a large amount of tests. The production of reliable data is a difficult endeavour. The management role that SpinOff plays in the work practices is also examined.

The factory related metaphors used by SpinOff computer scientist Calle to describe the general production process also seem to be of relevance when the work of the staff in the basement is analysed. In line with these metaphors, it is the work force, work processes, work organisation, end product, and raw material of the Obe trials that are in focus in this chapter. PharmaCo's protocol and SpinOff's computer control system both serve to make effective a complex production process with large amounts of "raw material" to process, i.e. participants, and data to produce. The data must be comparable, that is, of the same kind everywhere. The tools used to do this can therefore also be seen as tools to standardize and control the labour process.

The notion of there being similarities between a clinical trial and industrial production is not new, even though industry's role in the production of knowledge, as pointed out by Gaudillière and Löwy (1998: 5), has been of surprisingly small interest. Many of the studies have focused research and development, and been interested in how industry uses science to produce goods, rather than on "the know-how which contribute[s] to stabilize and to legitimize such scientific results in the laboratory" (Ibid.). The factory comparison has also been used when discussing how patients are treated in the health care system more generally.

Health care organisation has been likened to industrial production by stressing similarities such as the worker's instrumental view of her work, a work organisation built to bring about a production which is even and predictable, as well as the routine character of and detailed control over work tasks (Gardell & Gustafsson 1979: 113). More recent studies have also likened treating patients on the basis of scientific evidence with treating them as "mass produced objects on a factory production line" (Evans, 1995: 462 in Cronje and Fullan 2003: 353-354). The basis of these likenesses can be found in the rationalization of work evident in industrial work as well as in laboratory and clinical work.

One rationalizing tool that has gained somewhat iconic status in sociological studies of industrial production is the assembly line. The assembly line provides control over the work process in that it enables pacing and directing the work through impersonal technological means. In the Obe trials, the protocol can be likened to an assembly line, albeit a virtual one, in that it also paces and directs the work. This chapter looks into the ways in which the protocol and SpinOff's computer control system directed and paced the work of the staff in the basement in order to produce reliable data. It also looks into how the staff perceived the tools and their work.

In order to investigate the staff's work with these tools I make a distinction, following Fujimura, between production tasks and articulation work. A production task is seen as "a relatively well-defined task" (Fujimura 1987: 258) or "a standardized and repeated set of procedures" (Ibid: 260). It is contrasted to articulation work which is more difficult to define. Fujimura denotes articulation work as the different kinds of work done in order for the production tasks to be carried through, such as planning and coordinating the work (Ibid.). Following this distinction, I see the tasks defined in the protocol and computer system as production tasks, and the planning and coordination done to align the tasks to make the work process flow as articulation work. In the following, I will describe where the production tasks are performed as well as how the articulation work is done and by whom. Both kinds of work are needed in order for a clinical trial to be performed and reliable data to be produced. The kind of articulation work in focus in this chapter is the visible planning and coordinating of measuring devices, staff and tests taken, the kind of tasks that Hampson & Junor refer to as "visible, classical management work" (Hampson & Junor 2005: 168).

To access this articulation work one must enter into the very heart of the Obe trials: the basement. This is where the trial nurses and dieticians work, as well as where the trial participants go through the different stations specified by the protocol. It is "the shop floor" of the Obe trials, and it is here that the protocol's instructions are put to use.

The “factory” and its workers

Located one flight down from the reception of Centre University Hospital’s obesity clinic is the basement where the obesity drug trials are performed. The premises in the basement are used solely for drug studies and consist of a waiting room, four appointment rooms, a staff coffee room, a conference room, a few offices and a laboratory. The rooms were previously used for storage, prior to there being drug trials conducted in this part of the hospital. The renovation of the basement made it suitable as a work place as well as a reception for trial participants, and was paid for through funding from a pharmaceutical firm, the sponsor of a previous trial of another potential obesity drug.

By looking at the premises, there is no evidence of which specific trials are running any given moment, or that the premises are used only for industry financed research. The styling and design of the premises melt into the university hospital’s general aesthetics. The waiting room looks like most anonymous hospital waiting rooms, with a few chairs, tables and magazines. The examination rooms are equipped with the necessary devices for the drug studies, such as carefully calibrated scales, ECG equipment, a desk, a chair and a bunk. Occupying the offices are three dieticians, one secretary and four nurses.

It is in this basement where most of the events, or stations, specified in the protocol took place, and it is also here that the secretary, the nurses and dieticians involved spent most of their working day. Only two of the stations in the protocol – computer tomography (CT) and Dual Energy X-ray Absorptiometry (DEXA) – were located elsewhere, in the upstairs clinic. Other, internally initiated, research projects were also conducted upstairs. Since there were several drug studies going on at the same time, new ones starting up and others coming to an end, the use of the premises had to be flexible. During the intense screening phase of the Swedish trial, when 72 patient-participants passed through the basement per week, an additional part of the hospital had to be used. But during the succeeding run-in and maintenance phases, only the basement premises were used.

The premises used for drug trials were thus physically separated from the clinic. The upstairs and downstairs parts were also separate socially to some extent; the downstairs staff rarely spent their lunch and coffee breaks in the upstairs area. This spatial separation implied a notion of the downstairs activities being different from the upstairs ones. The boundaries between upstairs and downstairs were not rock solid, though. When a new project started up, or when extra personnel was required, staff crossed the boundary on occasion: a nurse working upstairs could be recruited to take part in a drug study or a nurse working downstairs

could be asked to help out in upstairs activities. These crossings were, to my knowledge, more frequent in the “going downstairs” direction.

One clinical trial nurse worked full time in the international trial, and one worked full time in the Swedish trial: Ninni in the former and Nora in the latter. The Obe trials also involved two dieticians: Denise in the international trial and Diana in the Swedish trial. Also, two different doctors, Maria and Martin, were assigned to conduct the physical exams specified by the protocol. The doctors’ production tasks were not full time and they did not spend their entire day in the basement, as the nurses and dieticians did. Both Maria and Martin had additional work tasks other than those in the Obe trials. In what follows, I will also at times refer to other doctors and nurses working with other research projects in the clinic. When I refer to the articulation work it is the research nurses that I am considering. There were other nurses helping out at times in the basement, but they did not coordinate or plan the work process.

Research nurses Ninni and Nora performed the majority of the production tasks in the protocol apart from the physical examination which was done by the doctor, the dietary treatment which was done by a dietician and the computer tomography and DEXA which was performed by nurses upstairs. Most participant visits (all in all 36 in the international trial and 25 in the Swedish trial) differed from each other, but some of the stations were passed through at every visit (see Figure 7.1). The participant saw the nurse and the dietician at each and every visit, whereas he or she, in the Swedish trial, only saw the doctor in seven of the visits. Also, in both trials, the CT and DEXA stations were only passed through four times during the whole study process.

The CT was run by two radiology nurses who specialised in these machines. They worked full time with the CT and performed the scans for other research projects as well, both external projects financed through pharmaceutical companies as well as internal projects financed through other means. One other nurse was in charge of the DEXA.

Dieticians Diana and Denise were each in charge of the “non-pharmacological therapy” station in the protocol. Their work consisted of giving the participant dietary advice and advice on exercise, something that was done partly, but not only, through the standard lessons specified in the protocol.

The doctor’s examination was also a station in the protocol, occurring seven times and distributed evenly in both the Swedish trial and the international trial. To some participants’ discontent, it did not involve the same doctor each time, and due to existing work routines for doctors, who did the examination at times varied depending on who had time at the moment.

The physical examination was a regular check-up, where the participants had the opportunity to discuss eventual side effects and also receive help with whatever other health related problems they may have had.

Producing inscriptions

The common traditional study is all about handling information. All you do is collect a lot of measurements and a lot of information, and the end result of the study is a pile of information, dated measurement results.

(Calle)

In the long process of finding a new drug, phase III trials are only one step, albeit a large and costly one. What is produced in a clinical trial can be seen as what Latour and Woolgar term inscriptions, “representations of scientists’ claims about the outcomes of their practice, sent to other places to convince and enrol allies” (Latour and Woolgar 1979: 50-51). I use the term to highlight that what was being produced was data derived out of participants’ bodies, which were the metaphorical raw material of the process. The participants’ bodies were measured and monitored through all the stations of the protocol, and in the process, parts of their bodily characteristics were reduced to inscriptions.

This process was done as the nurses, dieticians and doctors entered the representations of participants’ amount and distribution of body fat, blood sugar levels, etc. into the case report forms, CRF’s. A CRF consisted of two thick binders per participant, where sets of documents were kept for each visit. The same information was also entered into the participants’ medical journals. The material results of the trial process, the filled in CRF’s, were sent to the pharmaceutical firm where they were sorted, analysed and eventually turned into facts that would be sent to the Swedish Medical Products Agency (MPA) if the study turned out successful (i.e. showed high efficacy and tolerability of the drug) and used as proof of the drug’s efficacy.

The data, or inscriptions, stayed the property of the pharmaceutical firm once sent away from the basement. In that sense, as on many factory floors, the workers were alienated from what they produced. They worked with the tools of others (the protocol) to produce knowledge that they themselves did not own or control. Also the doctors were alienated in this sense, as they had agreed not to use the inscriptions in any way not previously approved of by the pharmaceutical firm.

The data produced in the trial were based on the measurements taken from the participants' bodies. In order for this raw material to be processed, it needed to be prepared. The aim was to have as smooth a production process as possible. This meant having a group of participants who, in addition to being a homogenous group with few health problems, were likely to cooperate with staff in a way that ensured they came to their visits in line with the requirements of the protocol. It also meant having participants who did not drop out of the trial. Thus, the group had to be a predictable one in order for the process to be smooth. The large scale selecting and recruitment of participants – finding the group of 541 participants out of 35,280 potential participants – can therefore, following the factory production metaphor, be seen as a way of selecting the homogenous raw material necessary for high quality data to be produced.

The nurses, dieticians and doctors each performed more or less standardized production tasks. The degree of standardization of the task was unevenly distributed for the three professional categories. The nurses' production tasks were most heavily standardized and the doctors' tasks were the least standardized. The dieticians' work was split into two parts: one that was heavily standardized and one that was not. The standardization of work tasks lends credence to the picture of the trial as an industrial production process, a view which is strengthened in the following section, where the focus shifts to understanding how staff in the trial viewed their work.

Routine and standardized production tasks

Each production task was specified and more or less standardized in the protocol. As an example, one of the regular short visits included six different production tasks to be performed by the nurse. It started with Ninni and Nora dispensing the drug to the participant, recording that he or she had taken the pills as they had been instructed, and, if not, recording which drugs were missed and when. The recording of drug intake was controlled centrally through an automated patient registration and treatment randomization system, the Interactive Voice Response System (IVRS). The IVRS was a system that randomized the participants who had continued to meet up with the entry criteria in visit 6 (see Figure 7.1) and adjusted the strength of the substance or dispensed a placebo. The randomization was done in a manner which was double-blind, i.e. neither the nurse nor the participant knew what the latter was receiving. The IVRS also recorded and kept track of if and when a participant had missed a pill.

The second task in this visit dictated that the nurse weigh the participant with standardized balances calibrated every three months, and with the participants wearing similar attire and at approximately the same time of day. For the third task the nurse took the participant's blood pressure, which was done using a wall-mounted mercury sphygmomanometer. The same size cuff was to be used each time and the participant should have rested for five minutes before the pressure was measured. Three consecutive measurements were to be taken. Fourth on the protocol was the pulse to be taken between the first and second blood pressure readings. Then, the nurse collected the participant's urine sample and finally she noted side effects brought up by the participant.

All these tasks were standardized, although to different extents. The giving and recording of the drug was minutely defined and standardized, as was the manner in which the weighing was done and the taking of blood pressure, pulse and urine sample from the participant. Recording side effects was also a well defined production task, although more difficult to standardize. Measuring a participant's blood pressure or body weight is a task that was relatively easy to do in the same exact way across the different centres participating in the trial. Such standardization involved using the same or similar monitoring devices at each site. For example, a specific and standardized scale and blood pressure cuffs were used across all sites.

The task of registering potential side effects, formulated in the protocol as "reporting adverse events", was however more difficult to standardize. What is considered a relevant indication to enter can be difficult to control across sites, although the protocol and staff I spoke with said that "everything" could be a potential side effect, and should therefore be reported. This specific task involved talking and listening to what the participants had to say and what they found important to bring up. These things could vary greatly: from having an aching toe to feeling queasy. The results from taking a participants' body weight can only vary quantitatively on a scale, while the results from asking about potential side effects is a question of kind and can be both variable and unforeseeable, and thus involves more independent judgement on the part of the nurse.

The production tasks in the protocol are many, and it is important that each detail of the task is done in the same way across the different sites in order for reliable data to be produced. Hence, there were many things to learn at the onset of each new trial. Nancy who had not worked with the Obe trials directly but had long experience from other trials, described these procedures in the following words:

The first time it's *a lot*, it's just loads of tubes and [...] you [are] supposed to know that "*these* tubes are to be turned for this and that time, and these are to be handled in *this* way". Some tubes are to be put down in ice at once after the sample has been taken [...] So, it's a little procedure before you learn how to handle the samples. And it can be different at the different visits. Sometimes maybe there's only a few samples to take, and sometimes it's the whole battery; when it's an important visit in the study where you collect a lot of data.

(Nancy)

These lab procedures were to be done in a very specific manner and in the same way in all participating centres, something that is made possible through instructions that were specified in the protocol. For every participant and visit there was a pre-packaged lab kit labelled with the visit number and all the information needed on what bodily fluids to put in which test tubes. This lab kit came with the needle and the test tubes needed for the visit. In the pre-packaged test-tubes the eventual additives had already been added. For example, if a haemoglobin test was to be taken, the blood was put in regular, empty test tubes, whereas if blood fat or electrolytes was to be measured, it was done through separating white blood cells from red blood cells and the serum was put in a special type of test tube containing a certain liquid. The samples also needed to be stored in a way that did not damage them; usually this meant freezing the samples in carbon dioxide ice. The next steps, concerning routines for handling urine and blood samples were also, and for all drug trials in the basement, standardized and specified in specific lab manuals referred to in the protocol. The samples were taken into the lab room where some were centrifuged to separate out the serum. Also here, everything was specified, down to which transport firm was to be used for transporting the numerous samples to the central laboratory, which in the case of the international Obe trials was a contract research organization (CRO) in another European country. Finally, the nurses packaged the samples and sent them to the central laboratory, something which often was done on a daily basis, planning for and taking into account that the central laboratory was open when the package arrived, so that the samples did not risk being spoiled.

From this description of what is done in one visit in the Obe trials, it becomes evident that each visit is broken down into many detailed production tasks. The many details are, however, not brought up when Ninni, who was the trial nurse in the international trial, talked about her work tasks. Instead, she gives the impression of a simple and unskilled job:

I think anyone can do this job. All you do is measure pulse and blood pressure; it's really a work for an assistant nurse. And then just ask these questions about side effects... it's absolutely not any advanced stuff.

(Ninni)

It seems that once the nurse had learned all the details on how the protocol specified the tests to be handled, the details became routine work. The handling of the samples was taken as self-evident and not worth mentioning as something interesting. In the interviews when I asked the staff to give descriptions of their work, the production tasks were not a topic that spontaneously came up. I found this surprising considering the many tasks specified in the protocol.

I found that the nurses did not discuss much the details around the production tasks. The work seemed to be something they just did without getting too involved. And, perhaps since I entered the field when the trial had been going on for a while, eventual problems in doing what the protocol prescribed may have been solved. Since there was little talk or questioning of the protocol during the time I spent in the basement, my impression was that the work with it went along routinely and smoothly. I was told, however, that staff in other centres were more critical towards specific details in the protocol.

The staff's work with the protocol can be compared to what Wenger (1998) writes about how staff related to protocols in a different kind of setting, namely insurance claims processing. As for claims processors, the protocol can be seen to contribute to a broader experience of marginalization for nurses and dieticians, in relation to the researching doctors and the pharmaceutical firm that sponsors the trial. It signals that they have little to say about how the trial is being conducted. So, following Wenger, they understand what the protocol signals to them in terms of their position within the hospital hierarchy. Trying to get involved in details surrounding the protocol, such as whether or not it is designed in the best way possible, is therefore something that they are not very interested in. What the nurses and dieticians "learn" cannot be categorized into clear pieces of information of specific skills that are useable or not. Learning a job also means learning to what extent they should be involved in things such as a protocol and what to do if they run into a problem of some kind. They learn where to draw the line between what they need to know to do their job and what they do not. They learn to live with a degree of not knowing other things. And they learn to follow certain rules and do away with others, as well as to be engaged in some issues and not others (cf. Wenger 1998: 40-41). In Ninni's words:

Well, there is a bit of hierarchy in this. You work on the floor, so to speak, when you're a nurse. You do everything you're told to. You're supposed to go through all the stuff in the protocol, and everything else. And then there is someone who controls my data, and someone controls her data...

(Ninni)

The instructions in the protocol are seen as something that, to a large degree, guides or controls the work process and as something that one is "supposed to go through", and is then controlled higher up in the hierarchy. In the international trial, the pharmaceutical firm's monitor checks what has been entered into the CRF, on a monthly basis, to see to it that no data is missing and that there are no obvious errors. The data produced through all the production tasks are highly controlled both by the pharmaceutical firm, "the sponsor", but at times additionally by governmental authorities as well. Such authority "inspections" and "audits" are, on top of the monitoring performed by the pharmaceutical firm, routine in clinical trials, and serve to control that the data produced are reliable, and that the documentation is in order, but also to safeguard the participants' participation, something done by controlling that informed consent has been collected. This explains Ninni's sense of extensive control of the data produced, where the protocol is just one part of the control.

Dietician Denise, who is responsible for the "non-pharmacological" treatment in the international Obe trial, shares a similar view of how the protocol affects her work practices:

Well, we get a protocol that is to be followed in our hands, and that's what it's all about. To strictly follow it and see to it that this is done in the manner they want. And if there are any uncertainties, you have to find out and ask "what do you mean here?". So it's... it's already been written, so there's nothing we can do about it.

(Denise)

As Denise indicates, the protocol largely decided what was to be done. She had to "strictly follow it and see to it that it was done in the manner they wanted". Interestingly, she shifts in the same phrase from referring to the protocol as a non-human actor – "it" – to a more diffuse and human "they". This connotes a sense of there being implicit goals and interests behind the protocol, the goals and interests of someone else. Therefore, if there is uncertainty when it comes to some detail of a production task, Denise says "you have to find out and ask", something that points to the possibility of there being different judgements of the same description of a specific task.

The nurses also mentioned that it is never possible to have a tool that standardizes all work. It is inevitable that one sometimes misses some of the many production tasks to be done. The nurse may simply forget to weigh the participant, for instance, or participants may forget to hand in their samples as they had been told to do. In a more subtle way, the process is not standardized since different nurses listen to blood pressure in different ways and pull the measurement tape more or less tight. It may also be practically impossible to weigh the participant at approximately the same time of day at each visit, since it may not be possible to schedule each participant in such a smooth way. A one hundred percent comparability can not be reached in practice, even though the production tasks are defined in a way that would seem to imply this.

When it came to doing the work of filling in the data derived from the different production tasks, medical doctor Martin emphasized the protocol's "tedious" and "boring" characteristics:

...it's *so boring* to sit and fill in these protocols; it's totally brain dead filling them in day in and day out. It makes you totally wacko at the end of the day. I mean, like the nurses: they know the numbers of the patients...their codes...you don't mention the participants by their name but with their code.

(Martin)

The extensive work of filling in the CRF binders, in combination with the notion of there being "nothing to do about it", gives the sense that the staff have an instrumental relation to the protocol and CRF as part of their work. It is an instrumental relation in that they work with and use the protocol and CRF in order to get the job done, but that it compromises, to some extent, their clinical practice of relating to the participants as individuals with names. In this sense, the protocol makes the work instrumental. It is a tool used only to produce reliable data.

These descriptions show how the work processes are seen as controlled, routine, detailed and standardized to an extent that, for some, makes the work unattractive or tedious. Nurse Nina compares her work with drug studies to the patient related work she is familiar with from experience working in the clinic upstairs:

It feels a lot freer to work with patients, so to speak. Well, I don't know what it is... maybe because you can't have a say. You can't have an influence on a study [...] because everything is decided beforehand... what to do and... even if you think some things are a bit off. Yeah, it's probably because you can't have an influence on what you do.

(Nina)

Here, Nina says it is “freer” to work with patients in the clinic since it allows for greater control of how the production tasks are to be done. It is important to note, however, that staff had a part, however small, in shaping aspects of the protocol's design. The degree to which they could do so was different between different research projects at the department. In drug studies in the basement there was an already finished protocol whereas in internal studies in the clinic there was more room for the nurses and other staff to be part of shaping the protocol. In Nicole's words:

In the internal [studies] you get to take part and have an influence yourself. You get to participate from the start and do some planning. “We want to look at *this*, *this* and *that*. Do we have something to add or should we get rid of something? And time frames... how much time do we put for each patient?” and so on. Well, you're more there from the start. Not in everything... you don't raise a thought, that's mostly the doctor's and professor's [job]. But later... you get to participate and have an influence on things... how many millilitres of blood you need and so on [...] how many test tubes to take... take part and design a little yourself.

(Nicole)

From what Nicole says, being able to shape the protocol meant being part of the planning of the work “from the start”. If there was something that the nurses wanted to add to the protocol or something that they saw as too difficult to follow through in practice, they had the possibility to do so as far as internal studies were concerned. In internal studies, the organization of the time needed was scheduled for each patient, and estimation of the amount of time each production task would take was work that was not only an issue for the research doctor. The nurses were not only left to follow a protocol even if the initiative to the study and its major goal was not defined by the nurses.

Managing the production tasks

The kind of work that involved time estimates and organizing or scheduling is different in drug trials and internal research projects not involving drugs. Working with an internal study was more like being one among many others in the clinic, one of the nurses told me, and the work is more demanding in terms of work load. It was seen as advantageous, however, due to the possibility to shape the design of the protocol. But not everyone agreed that internal projects gave one more freedom. Ninni held a contrary view, and said that working with drug trials involves more a sense of freedom:

You have your protocol, but then you draw up the work, together with the monitor. You follow *the protocol*, but you still have a say... how and when and where and so on. You can never do that in a [regular] clinic.

(Ninni)

There is some room for having a say in “how, when and where” the production tasks are done, that is to take part in organizing the production tasks. This type of visible articulation work seems to occur to different degrees between internal projects and drug studies, on the one hand, but also between different drug studies. In the international trial (which is what Ninni refers to above), the coordinating in terms of scheduling the work was done in collaboration with the monitor from PharmaCo. This gave more control over the “how, when and where” of the labour process. In internal studies these factors were controlled more by the research doctors as well as by nurses with managerial positions in the clinic. In this sense, working with a drug study was “more free”, or invertedly less controlled, than working with an internal project.

When seen in the longer term perspective, however, it is clear that the nurses have had some kind of effect on the design of the protocol, at least on the time and event schedule, or the work process part of the protocol. The kind of work done around the protocol has changed over a longer time period. This became apparent when talking with Nadia, who had worked many years with clinical trials. She spoke about how the clinical protocols have changed from when she started working in the early 1970's, from being a few sheets of paper with relatively rough instructions, to the 85 pages of the Obe trials three decades later. The protocol was not as detailed and standardized then.

When I started, all I got was a protocol and a recommendation to start at once. And once we started, it turned out that it was impossible to follow through. [...] There was no time for it. I can give you one example: We were supposed to do a [specific examination], and in this examination, the patient is supposed to lie down and rest for half an hour before you do the measurements. But that wasn't all. You also had to take blood tests and blood pressure, for instance. And then they're supposed to stand up for five minutes. And I was supposed to do this once every half hour during the first two hours. So, you can imagine... It was impossible to follow through. No chance. These are the things you know, being a nurse.

(Nadia)

This older protocol that Nadia talks about did not take into account the time it takes to perform all the tests that were supposed to be done, it only specified what was to be measured, but it was not rooted enough in real practice, which may point to the relation between nurses and protocol designers not being a very close one. The nurses working in the trials have been a part of these changes. The citation can be interpreted to show that the nurses find the protocols easier to follow today, and that this is due to the changes that they themselves have contributed to.

One way in which the staff exert control over the protocol, at least in the long run, is to call attention to the practical difficulties of carrying through a study. Through incorporating the experiences from the clinic in the design of the time and event schedule, the standard forms of protocols have changed over the years. The experience from practice gets incorporated into the design of the protocol, at least in the long run. Lessons about the everyday work practice learned in one trial can thus be taken into account in future protocols.

In the Obe trials each production task, as we have seen, was well defined and standardized. The physical examination was the only production task whose contents were not explicitly defined more than that the doctor was to perform a "physical examination" in seven of the twenty-five visits in the Swedish trial. Doctor Maria did physical examinations in both Obe trials. She had no overarching responsibility for the trial, but was responsible for the individual participants' health during its course. She talks about the examination or production task as not always feeling "meaningful":

It's not much work there but it's in a way... it doesn't always feel meaningful... It's a different role than sitting... like Magnus [the "principal investigator"] who doesn't see the patients that much. What I liked about [another drug study], was that you had all the pieces.

(Maria)

Here, the difference between the doctors' roles in doing research and clinical duties, respectively, become apparent. Doing the background work for a large research project such as the Obe trials involves tasks such as finding centres willing to participate and working with budgetary issues and ethics committees, also an example of visible articulation work of a traditional managerial kind. This is engaging work and involves responsibilities over the project as a whole. Doing a production task in the basement, such as the doctor's examination, on the other hand, is likened to "not having all the pieces". Being a doctor in the trial does not automatically imply much greater control over one's work process than it does for a nurse or dietician. That depends on where you are standing in relation to the metaphorical production line.

"Better than routine care"

Routine, standard and at times prosaic as the production tasks may seem, many in the staff still see their work as more attractive than routine hospital care. Since all Obe trial staff had worked in the Swedish public health care system before or parallel to working with clinical trials, public health care became a natural point of reference when talking about their work. In order to understand what they thought about it, it was therefore important to know with what they compared the clinical trial work. Ninni described some of the reasons why she liked to go to work:

We always have a good time together and there are many good things to say. I mean, that's why you're still here. [...] You [...] make your own work schedule... you can come late if you need to, and you can take some time off. So there are many advantages.

(Ninni)

The friendly and welcoming atmosphere in the basement was one reason why the work was attractive, something that several staff talked about. Also, the work enabled them to have flexible working hours, which was not common within the rest of the health care system, with

pressured and stressful work situations due to downsizing and lack of stand-ins. Although the job implied that they had to work more during times of high work loads, they could compensate for this by working less at times of low work loads. Such flexibility was something that was valued by staff who were used to working in shifts that involved work on nights and weekends.

It's very attractive [working with drug trials]. Partly since it is daytime, mostly. And you get to do somewhat different things, things that are a bit more fun. Today's health care isn't that fun, with cutbacks and high pressure and no stand-ins. There's a lot of pressure...which makes things like this even more attractive.

(Nadia)

The job has advantages in that it is daytime work and that one can do "different and more fun things". These fun things are placed in contrast to the less fun aspects of being a nurse in "today's health care system" with high work loads and downsizing of the health care sector. The increasing pressure in the public health care system is a recurring theme, used as an explanation to why the work in the basement with less pressure and more flexibility is more attractive. But its flexibility also implies an increasing reliance on temporary work conditions such as project-based employment. Part of the staff recruited for clinical trial work is there on project basis. Nadia again:

You don't have a permanent employment. Those of us who have worked since years back [do]... There aren't any permanent posts. Today, everyone is hired on a project base. So it's even more insecure. And there's been a lot of turbulence lately, because if there aren't any studies, you can't keep the staff.

(Nadia)

Attractive as it is, the job also comes with insecurity in the shape of project based employment. So, when it comes to the attractiveness of clinical drug trial work, there is some ambivalence.

Project based employment is not the only job insecurity issue, however. If a drug study is terminated before schedule, due to things that are out of the control of the nurses, their employment also terminates unexpectedly and before term. In the Obe trials, one such cause was the study participants' unexpected side effects of the drug. In general, not many phase III

trials are completed “per protocol”. In the ten different Obe trials performed globally, only one was completed before the shutdown. In the case of the Obe trials, Nora in the Swedish trial lost her job when the trial was shut down.

Another aspect of why clinical trial work is more attractive is that it is seen as less routine. “Regular nurse work” at the clinic is even more routine, according to Nicole who explains what she means by routine work in the upstairs clinic like this:

You take tests before the doctor’s appointment, and then there is another doctor’s appointment and then you get a new appointment within three months and again you take the tests and then there’s the doctor’s appointment. And it’s almost always the same tests that you take [...] Everything goes along the same tracks so to speak.

(Nicole)

Thus, both work at the clinic and work in the basement consist of many routine work tasks. The difference seems to be that in clinical trials there is a change between different projects, which accounts for some variation, however small. Nicole continues:

But in research... When this project, this study is over, hopefully something else comes along... *Something different.*

(Nicole)

Getting away from seemingly never-ending clinical work tasks and being part of different research projects contributed to making work in the basement attractive. Another considerable advantage of working in drug trials were the fringe benefits that the staff received from the pharmaceutical firm. These benefits ranged from kick-off meetings abroad, to smaller lunch meetings, to presents at Christmas, Easter and summer. It is well known that doctors go away to conferences and on other kinds of trips, often to interesting locations. What is perhaps less known is that these trips, with expenses paid, involve all staff categories in clinical trials, not only the medical doctors. Dieticians, DEXA and CT nurses – everyone involved in the Obe trials, were invited to “kick-off’s” and “start-up meetings” by PharmaCo. Martin, another doctor whose job in the Obe trials was limited to the production tasks, also mentioned the fringe benefits of working with drug studies, and how he thinks this creates loyalty on behalf of the receiving staff:

Health care staff are not used to getting anything extra... [...] The contacts with the pharmaceutical firm is the only [way] to get this small... sort of gold-rim... I mean, like sitting there as a nurse in some boring reception... that someone in a fancy suit comes and treats you with a sandwich.

(Martin)

Here, Martin emphasises the fact that health care staff is not used to these kinds of benefits from working in the public sector. Working in clinical trials therefore offers a different and quite contrasting work experience to staff groups. Martin continues:

It's a different world. You meet a *business* world there... I mean [imagine] health care staff going about in their dull attire for weeks on end, and then suddenly they get to go away on one of these trial meetings and stay in *luxury* hotels and all that... which does not cost them *anything*, but does create a kind of loyalty.

(Martin)

In relation to the extreme cost of running a large scale clinical trial, inviting the whole staff group in 20 or 40 different centres to stay in luxury hotels involves relatively limited expenditures, but the benefits in terms of increased loyalty among staff are, Martin implied, considerable.

Hence, the repetitive tasks of filling out of forms and the controlled character of the work is outweighed by an increasing sense of freedom in comparison to what is referred to as “routine health care”, and the fringe benefits. The friendly atmosphere in the basement and the sense of belonging to or having contact with a “business world” also seems to add to the appeal of working with drug trials.

Making production flow through coordinating, planning and organising

We have seen how the protocol was a tool that specified what tasks were to be done, how they were to be done, as well as roughly specifying at what point in time. The multitude of tasks, stations and staff involved in a clinical trial means there is a need for planning and coordinating the production tasks, if reliable data are to be produced. Nurses do more than just carry out production tasks in line with instructions in the protocol. They also coordinate between staff, tasks and equipment in the different stations in the trial. Here, Fujimura's

distinction between production tasks and articulation work becomes useful. She defines articulation work as:

...the work of pulling together everything that is needed to carry out production tasks: planning, organizing, monitoring, evaluating, adjusting, coordinating and integrating activities (Fujimura 1987: 258).

We now turn to how this articulation work is done in order for the production of reliable data to flow smoothly. Here, I will focus on the narrower type of classical managerial work done by the nurses and dieticians in the basement (i.e. planning, organizing and coordinating). This type of work is of a kind that is, per definition, not mentioned in the canonical accounts of work, in handbooks or in the protocol. Natalie talks about this work in terms of making things “flow” in practice:

We need to follow it [the protocol], but [...] organize the work for it to flow well in relation to the participant’s appointments with nurse, doctor, and that the examination rooms were free, and that the material used was available, and that it was practical and that it would take as little time as possible.

(Natalie)

Seeing to it that a room is available or that the participant does not have to wait too long between seeing the nurse and dietician are examples of articulation work. The articulation work needed for the protocol’s production tasks to be performed is illustrated in the following description of what the nurse has to do in one of the stations or visits.

In visit 16 in the Swedish trial where the oral glucose tolerance test is done (OGTT in the time and event schedule, Figure 7:1) which measures blood sugar level, the protocol says that it is important that the participant arrives to the basement while fasting, that is without having eaten anything for at least eight hours. The nurse has to plan for this visit by informing the participants in the previous visit about what is expected of her in visit 16. In so doing, adjustments are made to individual participants according to potential upcoming concerns or questions. Such concerns include issues such as what she can and cannot eat before coming.

When the participant arrived, the first thing done was to take the blood tests. It was after this test that the glucose tolerance test was administered. When the sugar fluid in this test had been administered, the participant waited for 30 minutes before the new blood tests were taken. During these 30 minutes the participant was instructed to take her clothes off in order for the nurse to take the ECG. She placed the 12 recording leads at the specific locations on the body and recorded the heart activity into a small box. The results from the ECG were then sent over the telephone line for analysis by the contract research organisation (CRO) The equipment for sending the information in the small box to the CRO was located in the lab room, so the nurse had to go into another room to send the data. The nurse also used the 30 minute wait to measure “waist hip ratio” (WHR) and to weigh the participant.

This is all and well as long as everything goes along smoothly and without any mishaps. Reality was not always so simple, however. The telephone line to the CRO in the United States could be busy for 30 minutes, for instance, something that I was told had happened a few times in periods of intense work loads where all participating centres were trying to send their ECG results at the same time. When this happened the nurse had to decide whether to wait in the lab room until the telephone line became free, or to go back to the participant lying in the examination room and measure the waist hip ratio and then run back to the lab room to see if the line had become free.

(adapted from fieldnotes February 28, 2002)

Further, I was told that the participant was disconnected from the ECG equipment before the nurse went into the other room to send the ECG. But, after incidences where the measurement “disappeared” from the small box on the way to the telephone, the routine (at least for Nora) became leaving the participant with the recording leads, so that a re-measurement could be done quickly in case it had to be redone a second time. Falling behind in schedule may not always be a problem, but if there is another participant waiting her turn, or if there is an extra patient squeezed in the same day because she missed her earlier appointment, the whole day’s schedule will be disturbed and the day becomes very stressful. Being able to adjust to *ad hoc* situations that occur is therefore important for the work to be done.

Coordinating the different staff and stations to make the process flow is also important. In the larger visits, such as visit 16 where the DEXA and CT were performed, coordination had to be done with the nurses upstairs to see that they and the equipment were prepared to let the participant go upstairs. Also, somewhere among the numerous production tasks, someone had to see to it that the participant filled in the “quality of life” questionnaire. This was administered either by the nurse or by the dietician, depending on who had the time.

Since there are many different production tasks to be done at each visit, each visit had to be planned in advance in order for production to flow smoothly. Especially when it came to the more extensive visits, there was a need to do some reviewing beforehand, in order to remember what was to be done, one of the nurses told me. To help remember all the details and structure of these visits one of the nurses who worked at the beginning of the international trial had made templates in Swedish where all production tasks at each visit were specified, making it easy for the nurses to quickly check to see that all tasks had been performed. The time and event schedule gave a rough picture of what tasks were to be done in a particular visit, but for information as to in what order they were to be done, staff had consult the protocol. Thus the information provided was not sufficiently well organized to make the production tasks flow.

This description indicates the role of the articulation work involved to enable the production tasks specified in the protocol. Coordinating the materials used and the different staff groups and thereby seeing to it that the work around the protocol runs smoothly – articulating the work process – is an important part of the research nurses’ work to make the process flow. It is evident that there is a considerable amount of planning, organizing and coordination needed for a successful follow-through of the activities in the protocol.

Computer based organizing and planning

When it comes to planning and organizing the work tasks there is one significant difference between the international trial and the Swedish trial. In the international trial, trial nurse Ninni made her own templates to follow in order to remember all the details of the protocol, something that may have added to her sense of “having a say, however small”. In the Swedish trial, however, the part played by PharmaCo’s monitor and Ninni in organizing the details of the work was partly replaced by SpinOff’s computer control system. The planning, organizing and scheduling – the “how, when and where” – was something that SpinOff controlled through their software. Thus the articulation work of what Calle referred to as keeping up with the state of the process was in the Swedish trial no longer part of the research nurse’s job.¹²

¹² The extent to which this was so, and how the computer control system affected the work in practice, is not possible for me to explain from the data I have collected. Only one of the nurses – Nora, who was trial nurse in the Swedish trial – worked with the computer system in the basement. She was obviously under pressure when I

Calle, the computer scientist at SpinOff, made a distinction between process data and analysis data, where he said the former is “steering data in order to control the flow”. A smooth flow implies participants come to their scheduled visits at certain intervals and the nurses, doctors and dieticians succeed in doing all the standardized tasks prescribed by the protocol within the same time frame. The process data is the data needed in order to make possible a smooth “flow” in the production process. Knowing where each participant is in the system, what tests have been taken and which ones are missing is crucial in order to produce reliable analysis data. This was done by the computer.

Concretely, the process data took the shape of what staff called a “time window”. A time window is the time frame within which the protocol defines it as ok for the participant to arrive for her visit. For example, the Swedish trial’s time window was three days before or after the time specified in the protocol. The computer control system helped to keep track of where the participants were in relation to the time window and what parts of the protocol they had passed through. In this way it was possible to have an overview of how the process was “flowing”. Calle explained:

We almost excel in creating this kind of process steering data in order to keep track of where we are – a different kind of information than the other results. It’s more data about how far we’ve come in the evaluation of this patient... “I care about what the values are, but the status is that we have gotten three lab values but are missing two, and that we have one survey in and one is only half finished”. That’s process steering information, while exactly what they answered on question two, is more analysis information.

(Calle)

Process data, steering data and flow data are terms used alternately and synonymously for information about if and when a participant has gone through the production tasks specified in the protocol. It does not include the results from the tests – only if and when, for example, a blood sample has been taken or if and when a participant has filled in the quality of life questionnaire.

did my fieldwork in 2002, and did not have time to be interviewed. When I tried for another interview in 2004, she also declined.

It's important to keep track of this state of the process in order to be able to decide what to do next... What is needed to take another step, and all the time push the patient through the system.

(Calle)

There were some problems with the implementation of the computer control system, due to the time windows being too small. The introduction of it in the Swedish trial brought with it some controversy down in the basement. For example, it was seen as “technocratic” by clinical doctor Martin:

There was such a technocratic structure over the whole thing. And in a way... an experience from the drug study, is this clash between care and industry, that [...] it is there you meet a person and it is there you realize that things take different amounts of time and that maybe it can't be done.
(Martin)

Using the term technocratic in a situation where patients are concerned can be seen as signifying there being different rationalities in caring for a person and organizing industrial production of data. Meeting a person means seeing to his or her individual needs and concerns; things that may take a certain amount of time. Individuals' needs and concerns are unforeseeable. Standardizing work where patients are concerned is therefore difficult. Through its computer system SpinOff refined the control of the flow of the clinical trial. But, in order for it to work, the system had to be adjusted for the complexities of real life situations. There were then constant changes made in order for the system to be as flexible as possible towards what “reality” looked like. Controlling the production process in 20 different centres with their respective staff groups demanded a system that could account for all the differences and diversions that were made in practice. Total control was neither possible nor desirable and the system had to be flexible as to what happened in the different centres if the accurate data was to be obtained.

We want to control centres, but at the same time we've realized that it is not enough to, like we did in [another study] say “this is the way, everybody march at the same pace, all patients forward now. Everybody should be here now.” There is always someone who says [weak voice:] “But I don't have that”. And you can't just ignore them. They've described a different way, really. Reality looks different. (Calle)

From previous experience of working with other large scale research projects, Calle and his colleagues have had to learn that the control system has to be flexible enough to incorporate all the unpredictable events that may occur in the basement:

There is always an element of control. We always want to suggest what is best: “book the patient here... no, don’t take the Wednesday, take Tuesday. It’s much better, then you’ll have some time in case something happens”. But if they’re stubborn and say: “no- it has to be Wednesday”, then the system has to say “ok”. [...] So it’s a combination of control, but with some sort of flexibility. (Calle)

This reasoning shows how SpinOff has tried to build in flexibility in the computer control system. Some things cannot be controlled centrally, they are always best dealt with locally at each centre. Therefore, control becomes more efficient if some room is made for the staff to make their own decisions. If a nurse forgets to enter one piece of data, a participant has forgotten to bring in her urine sample, or if a participant is unable to come to the visit within the set frame, the system must be able to handle these diversions. Each difficulty encountered is therefore taken into account in the continuous development of the system.

The extent to which staff was chained to an assembly-line-like protocol thus differed between the international trial and the Swedish trial. The staff in the international trial had more control of the flow of their work, in that the work process was organized together by the trial nurse and the PharmaCo monitor. In the Swedish trial, where SpinOff’s computer system controlled the scheduling of the work process, this – according to both Calle and staff in the basement – resulted in a much rigid time schedule.

The data produced in the trial can be analysed as an end product in the testing procedures. In order for the data coming out of the study to be reliable and of good quality (in line with the protocol), the production involves different kinds of work. First and most evident are the production tasks that are specified in the protocol. The nurses perform a multitude of detailed and standardized production tasks while the dieticians perform two, and doctors one. At the beginning of a trial, personnel have to learn a lot of details. Working in the trial involves remembering details and structuring the visits accordingly, and as efficiently as possible.

The production tasks are more or less standardized. I have showed that there is room for independent judgement where the less standardized tasks are concerned. The degree of standardization is not as high when it comes to the production task to be performed by the

doctor. But, being a doctor, as compared to a nurse, does not automatically imply greater control over the work process, with the exception of the research doctor who is responsible for the study as a whole and thereby can both influence the design of the protocol as well as publish articles on the results of the trial.

Most production tasks in the trial are very detailed and standardized, however, and thus discipline what is done to a considerable extent. The protocol and computer control system largely control what is done. It is perhaps easy to see why Calle, the head of software design in SpinOff, talks about the work practices in industrial line metaphors. The protocol, with its time and event schedule, can be likened to an assembly line. The protocol is already written, in all its details, when staff on the floor begin to work with it. The protocol also prescribes a certain number of stations to be passed through, as would an assembly line, and moreover similarly directs and paces the work through the time frames specified.

This chapter has also shown how the work is both controlled and hierarchical. The personnel are subject to both monitoring by the pharmaceutical company, or its auxiliary monitoring firms, in addition to audits and inspections performed by the Swedish Medical Products Agency. Their reflections about their work confirm this sense of being controlled, which can be seen as part of the reason why they have an instrumental relation to what they do. Thus, the chapter gives a sense of a work process that – despite some staff describing it as less routine than clinical work – is highly disciplined through monitoring, auditing, and a detailed protocol. In the case of the Swedish trial, work is even more disciplined through SpinOff's computer control system.

Local i zati on through compl i ance work

In order to generate useful data, the participants need to stay in the trial throughout the time specified in the protocol. Maintaining the participants' motivation to come to all the visits can be difficult, however. The participants may find the different testing procedures too extensive, and their motivation can wean during the course of the trial. This may be especially true if the treatment has little or no effect. Motivating participants to come to all the visits and making sure they take their pills, to ensure what in clinical trial terminology is called "compliance", is of crucial importance for the clinical trial to be conducted in an efficient and successful way.¹³

In order for compliance to be produced, the protocol has to be flexible enough to give a certain amount of freedom to the staff and participants. I will show how the staff treats the participants as patients to encourage compliance and, in extension, for reliable data to be produced. By analysing this work, a more complex picture emerges than the industrial production detailed in the previous chapter. The work involved in following the protocol's instructions is not just a question of performing all the production tasks and coordinating and planning the work to make the process flow. It also involves including the "patient" into the work: a participant with non-standard and to a certain extent unforeseeable needs and characteristics.

Produci ng compl i ance

Compliance is one of the many terms used in clinical trial discourse. It denotes how obedient or docile the participants are in taking the pills and taking them at the required times. There is not much written about compliance in the protocol; it is only explicated on one page, where there is a heading named "compliance", under which the following can be read:

¹³ Within the academic field of nursing, the concept of compliance has been debated for the last 20 years, nurses being critical towards its similarly negative connotations (see e.g. Murphy & Canales 2001 for an overview of the critique).

Compliance

The investigator or designated study personnel will maintain a log of all study drugs dispensed and returned. Drug supplies for each subject will be inventoried and accounted for throughout the study.

The number of tablets prescribed and returned will be recorded at each visit.

(clinical research protocol)

Compliance, as far as the protocol is concerned, means that the study participants take their pills. For the trial to be correctly done it was very important that every participant takes the pills and does not end his or her participation prematurely. The protocol even includes the production task of telephoning the participants prior to the visit to remind them to take their pill in the morning (clinical research protocol: 39). This explicit instruction in the protocol signals that non-compliant participants have been an issue and are anticipated in the study design. It is well known that it is more difficult to achieve compliance in a trial such as the Obe trials, where participants self-administer the drug at home, than in a trial where the intervention is in the hands of the trial doctors (Jadad 2000: 32). Trials where participants take a drug over a long period of time are also known to lead to lower levels of compliance than short term trials.

The instruction to remind participants to take the drug can be seen as constructing the participants as “forgetful” rather than having a low motivation to take the drugs. They may be interested and motivated at first, but find that later on in the study they do not have the energy or time. They may re-evaluate their reasons for participating in a clinical trial. Their interest and motivation are not constant. As a participant’s interest or motivation weans, the staff’s ensuring compliance to the protocol therefore becomes even more important, hence the instruction to remind participants to take the pills as instructed.

Oudshoorn, in her study of the development of a male contraceptive, brings up different ways in which investigators and clinicians work to make participants into reliable test subjects (2003: 175ff). This work involved providing them with attention and health care to an extent and kind not possible to get anywhere else. It also involved creating a nice, friendly and non-hierarchical atmosphere to make participation a pleasurable experience. Such work is evident in the drug trials in the basement, as well. The social atmosphere in the basement was warm, welcoming and friendly, something that many parts of staff mentioned, as well. This most certainly contributed to participants’ desire to come back, even though the atmosphere

perhaps was more a result of the staff feeling “more free” in their work tasks than they did in the upstairs clinic, as mentioned in the previous chapter, than the result of a conscious effort to make participants compliant. However, the staff intentionally worked with motivating individual participants to stay compliant, as described by dietician Diana:

In a study, as the one administering treatment, you're very adjustable, because we do want to make participants stay. They're here because we ask them to be. Partly. Well, they have an interest of their own, but that they follow these frames that are very... [...] We have to be happy that they do it. So you adjust to each participant as far as possible, if they ask for specific things, such as if they don't want to do certain things, then you find out if it is possible that they skip it, and if so, what happens then.

(Diana)

The participants, Diana says, “are here because we ask them to”, a statement that implies the staff and study designers should be grateful that they take the time to come to pass through all the stations of the trial. Participants do this partly out of their own interest to lose weight, but it seems Diana thinks the work the participants put in does not measure up to what they get; hence the expression that “we should be happy that they do it”.

All staff groups in the basement are very attentive to the trial participants' different needs in order to make them motivated to stay in the study, but, and provided that it is the nurses and dieticians who see the participants most often, it is on them that this responsibility primarily rests. The work of making participants compliant can therefore be added to the list of tasks not specified in the protocol but needed in order for the production of reliable data. Nina mentions how much work is put into making participants compliant to the study:

You do a lot with them. You're very keen on trying to keep them in the study. The firm wants that, of course. You do a lot for them [...], call and ask how they're doing. There's a lot of pondering to the participant.

(Nina)

The somewhat vague expression “pondering to the participants” signals the *ad hoc* character of what the staff do for the participants and that the manner in which this pondering is done is different depending on the individual participant's specific needs and concerns. Just following the protocol, then, does not work when dealing with individual participants. These individuals, homogenous as they may be as a result of the protocol's narrow inclusion criteria,

are not homogenous enough to be treated in one a standard way, as the protocol could be seen to imply. In fact, in order for the production tasks in the protocol to be done, the protocol needs to be open to interpretation. The staff need to be able to adjust to the participants to the extent that makes them motivated to stay on in the study. Berg has discussed how rationalizing tools, such as a clinical protocol, need to be “localized” in this way in order for them to work in practice (1997: 152). The tool disciplines practice, but only to the extent that staff judge to be appropriate. Practice, in turn, shapes the tool over time, as continuous changes and adjustments are made to the tool in order for it to fit better with practice.

In the following, I will bring up two examples of how the protocol’s production tasks are localized in order to produce compliant participants. One example shows how the dieticians digressed from the protocol instructions, and adjusted it to make the procedures more meaningful to the participants, and to themselves. The second example is taken from the work of nurses and dieticians, who perform counselling to participants for different problems related or not to their body weight.

Di gressi ng from the protocol

Denise and Diana, the dieticians who worked full-time in the international trial and the Swedish trial respectively, were in charge of the “non-pharmacologic” part of the treatment given to participants during the duration and follow-up of the trial. They followed the protocol, as the nurses did, and entered data into the CRF. But there was a difference in how detailed their instructions were in the protocol. Their work only involved two production tasks. The first was a standardized treatment that consisted of a number of “lessons” to be handed out and discussed at each visit. The second was an individualised part of the treatment where the participant was given advice concerning diet, behaviour and exercise.

What the designers of the protocol had seen as important was that the participants receive a treatment for their condition and that all participants in all locations receive the same type of treatment. The pharmacological therapy needed to be compared with another treatment in order for the comparisons between different participant groups to be conducted. Such a comparison is only possible if all participants receive the same treatment. The lessons were therefore standardized, so that each participant could be said to have received the same treatment. In practice, however, it was hardly possible to give the same dietary treatment to each individual participant. According to the protocol for the Swedish trial, “non-pharmacologic weight reduction therapy” was to be provided at every visit. When the

participants were enrolled, the dietician was to help them with three things: an “individualised nutritionally balanced diet”; a “behavioural modification program”; and an exercise program. The amount of energy of the prescribed nutritionally balanced diet was calculated to be 600 calories (kcal) less than what the participant was estimated to expend or use on a daily basis. Part of the production task was thus to calculate the participants’ daily energy intake and help them find ways to reduce it by 600 calories per day. The dietician is supposed to assist the participant in maintaining the calculated level of energy intake.

The behavioural modification program was the part of the non-pharmacological weight reduction therapy. It was standardized and consisted of a number of “lessons”. These, in turn consisted of corresponding brochures given to the participants, with topics such as “Why Lose Weight?” and “The Change Process: How, When and What to Do”. When the standardized program was introduced, it brought with it intense discussions among the dieticians and other staff working in the basement. The program was developed as part of company health care in the United States, which was one reason why it was not seen as applicable in the Swedish context. Moreover, when the written material arrived, it allegedly had flaws in the translation from English to Swedish. Therefore, the co-principal investigator hired a translator in order to make the program better. The result was still not satisfactory, however, according to Daniela, the dietician working at the research department, because the translator did not have experience or knowledge of the clinical situation.

Another problem with the weight loss program was that it was not developed for diabetes patients. This was considered a particular issue, since the participants who made the entry criteria in the Swedish trial were newly diagnosed with or had untreated type 2 diabetes. Dietary advice for people with diabetes, according to Diana, needs to include aspects other than those only related to weight loss. Both Diana and Denise were so sceptical towards the material at times that they felt that they did not want to give it to the participants at all, and in a few cases actually withheld the material, contrary to the protocol’s dictates. The individualized part of the treatment was seen as much more important.

The exercise program was individually designed by the dieticians and adjusted to individual preferences. But neither Denise nor Diana were very happy with the standardized “lesson” that the protocol prescribed them to use. Both agreed it was not well suited to the local context, nor did it fit each individual situation. The clinic had extensive experience in working with overweight and obese persons, and the use of a standardized protocol, or parts of a protocol such as “the lessons”, was therefore problematic for the dieticians involved.

Another problem, from the dieticians' perspective, was that the data collected according to the instructions of the protocol did not indicate the circumstances under which the participants had attained their excess weight. These circumstances vary enormously between individuals. Some eat too much out of life-long habit; others eat too much chocolate, for example, to satisfy a dependency or produce feelings of comfort. Yet others have what can be characterised as eating disorders.

According to Diana, the standardized lessons can be of help to the participants, but only to a certain extent. This is because each participant with their individual eating histories, need an individually designed treatment. This is how dieticians are used to working. In the CRF, all that had to be entered was whether or not the dietician had handed out the material and whether or not the participants had "done" their lesson. While the nurses enter significant amounts of information into the CRF, Diana and Denise only tick two boxes. This does not mirror what they actually must do during the treatment. According to Diana;

[the boxes] only say whether or not I've handed out the material or not, and if the patient has done his or her lesson or not. But, not having done their lesson does not have to mean they haven't done good things with their eating. So it feels sort of... It's only a formality filling in those boxes.

(Diana)

In the CRF, the wide range of issues raised in dietary treatment is reduced to these two boxes. As not only obesity is treated, but also type 2 diabetes, the standardization of the dieticians' work seems to reduce a complex job significantly. The data entered in the CRF did not say anything about if and how the participants had made changes to their eating pattern.

Thus, the diversity of the work involved in dietary treatment is made invisible. Most parts of this work are not apparent in what is entered into the CRF. However, the dieticians make the protocol work for their practice even while maintaining an instrumental view of it. They make it work through giving less importance to the standardized lesson, and at times skipping it completely. Sometimes, when a situation occurs where the dieticians feel uncomfortable with the standardized lessons, they deal with this by handing it out, but not talking about it. Sometimes they do not hand it out at all. Instead they choose to talk about what they judge to be of most help to the participant at the time, or they talk about other things needed for the participants to stay motivated. These motivating factors can vary widely, which I will discuss below.

Counselling the participants

One part of the staff's work that is not visible in the protocol or the CRF, but important for motivating patients and thereby to make the tools work, is the counselling of participants. The participants often bring up issues they want to discuss or receive help with. Losing weight involves issues concerning appearance and finding a healthier lifestyle. One of the nurses vividly told me about one of the female participants who had lost a lot of weight and how this affected her feelings about herself; she thought her thinner body gave her a "different kind of respect":

Sometimes you feel that they are panicking, like "help, help, what can I do, you have to help me". But we can't do anything sitting there on the chair. But then you saw... really fun things... those that lost maybe 20 kilos and turned so splendidly smashing and spoke of how people turned around to look at them on the street when they saw them. That had never happened to them in their entire lives... [they] get a totally different kind of respect everywhere... [They] start to wear make-up and buy new clothes, and life becomes all different. Those things make you really happy. It's great fun.

(Ninni)

What often engaged staff, as illustrated by the quotation above, was to follow individual patients and their progress or problems. Thus, it was not only the issues raised in the protocol that were taken into account in the situated staff-participant encounter, but wider sociocultural and even psychological issues.

Discussions arose between nurses and participants around what kind of new clothes to buy to fit this higher status and thinner body. I was for example told that one female participant felt uneasy with the clothes available for thinner bodies in that they were "too revealing". She had been used to sweaters that were big enough to cover her hips and backside. The dieticians or nurses were not trained or supposed to handle some issues like this. Denise dealt with such situations as follows:

I usually say [to the participant] that we can talk about whatever we like. And all that happens to them in life affects them and the extent they can change their eating behaviour and spend their energy on that. It does demand some time and planning and so on. And if there are things that are happening around them, then of course they can talk about it. Sometimes there is no room to talk about anything else, but we do see each other so many times. It can be good, if you want to, to talk to someone who's a little neutral.

(Denise)

Since eating behaviour is related to “all that happens to them in life”, many different issues may be taken up by the participants. Many events can affect the participant's motivation to change their lifestyle. Also discussed were problems they had that affected their appetite, how much they ate and why. Participants feel up or down, have problems with their close relations or at work, and some of them take the opportunity to bring these up. To talk about these parts of their lives in the visits is often unavoidable. But Denise points out that she has to be able to draw the line:

But sometimes you need to point out that I'm not a therapist or anything, when it comes to those things. What I can do is listen and be a fellow human, but I can't be some kind of therapeutic... help them on a therapeutic level...since I don't have that kind of education. It's more about listening and being present.

(Denise)

Nevertheless, this is the role she feels some of the participants assign to her, something the nurses and clinical doctors mentioned as well. This role can mean ending up in a situation similar to psychological therapy. Denise explained how she reasoned when she drew the line between what she can and cannot do:

What counts is finding a reasonable level, because you can't be a friend either... If they want to talk about something that has happened to them, then they may [...] but you can't be some kind of sink that you can pour anything into, either. I can't help them, and I usually point that out to them if I feel there's a need to... that I can listen and so on... and that we talk about what we like... but that this is something that I can't help [them] to solve. And maybe ask them if they've thought about looking for some other kind of help in that case. And we don't have that kind of help to offer here, through us...

(Denise)

It is up to the dieticians in the trial to find “a sound level” from which to handle the participants’ diverse problems. The words Denise uses here – “friend”, “some kind of sink” and “fellow human being” – show what roles she ascribes to herself in this relationship, but perhaps also signals what the participants feel they lack in their lives more generally.

While some participants have personal problems to discuss, others may, after many months of participation, have realised that they did not find losing weight that important after all. In these cases, Diana says, they end up discussing why this is so. Keeping these participants compliant requires a different strategy:

In those cases I don’t sit here and give advice. Instead, we talk about the material they get and then it’s, “thank you and good bye and be well until next time”. So it’s not an active treatment. You only deal with the study part, but it’s not anything active, really. And in that case, of course, you feel less meaningful, in a way.

(Denise)

Denise here draws an interesting delineation between “active treatment” and dealing with “the study part”. “The study part” is equivalent to the procedures specified in the protocol and is seen as less meaningful than “active treatment”. This demarcation of “the study part” from the more meaningful active treatment can be analysed as their way to safeguard their identity as dieticians as well as safeguarding their professional autonomy. It involves being able to analyse each patient’s individual needs and make their own, informed, decisions as to what advice to give the patients. Such work is more meaningful, also for the participants, than if they strictly followed the protocol.

All this shows the amount of “extra” work done in order to make the participants compliant to the protocol, a kind of work involving considerable discretion and individual judgement. What I want to draw out from the examples above is that the protocol is individualised through the digressions made from it, and that the counselling of the participants that took place is also a part of seeing them as individuals with specific needs. Such work is important for the scientific credibility of the study, since a trial where many participants have dropped out does not give much credibility to the data that is being produced. Here, the nurses and dieticians play an important part in making the visits meaningful and pleasant and thereby capable of producing continuous data. Martin even stated that it was this work outside the protocol that makes participants want to stay in the first place:

They wouldn't come if it only was this binder that lay there and they were to tick off a box. And if the nurse was brusque, they wouldn't show up either. They come because they get this contact, health care staff – patient, except it's really *trial* staff. And it is this which is later ...*exploited* may not be the right word... but in a way *used* in the whole system.

(Martin)

The personal relationship between participants and staff is what the participants' loyalty to stay compliant becomes based on. Hence, it is postulated that the participants would not be as compliant if it weren't for the "extra" work done by staff in the basement.

The Swedish speaking personnel did not translate the English term "compliance" into Swedish, but used the English word, which suggests it is being used as a technical term strongly connected to the practices of a clinical trial more than as a term describing participants' actions in relation to their conditions. The term is not uncontroversial, though, and seems to imply different things depending on the context. Dietician Daniela gave her view on what it means to be compliant, one that differs from the technical definition in the protocol, by saying:

I think it's very good compliance if they get a process of change started at all. If they do anything at all.

(Daniela)

Compliance for Daniela is not just about the participant taking the pills on time or not. Rather, she relates compliance to the work involved in making participants willing to change. In this use of the term, it is whether or not the participant starts to change his or her lifestyle that is most important.

Some can eat exactly the same thing day in and day out, but after a couple of weeks they get tired of it, and then it's not possible. Rather, it's all about finding your own way to relate to food and do the changes that you feel... "I can manage this, it doesn't feel like a sacrifice, I can do this and have it like this for the rest of my life". You have to have that feeling. And it's... the capacity to find these things and the will and capacity to look for and try new things... try to go different roads. That's what I think compliance is about.

(Daniela)

This shows that Daniela's work is a lot about teasing out what would work for the individual participant, and to help him or her find his or her own motivation to do just that. Compliance, to her, is about the participants being co-operative and motivated in changing their eating habits and exercise patterns – part of their lifestyles, really. Implicit in this line of reasoning is that what matters in the longer perspective is not the amount of weight lost in a certain time period, but the changes made by the participant him or herself. Changes in eating patterns are not possible to make overnight, and the participants have to feel that the change will be something they can live with without it feeling like they have sacrificed something in order to deal with it. Small, slow and long term changes are better than large scale and sudden changes, which are difficult to stick to. This is a motto that staff often referred to.

In contrast, what is interesting to the protocol is the amount of weight lost during the trial period, not what has happens to the patients in terms of motivation to improve their lifestyles and health. Hence, there are two notions of compliance at play in the trials. One is measured by if the participant has taken her pills and, if so, on time, and the other notion is concerned with each participant's personal way of finding motivation to change their lifestyle.

Different rationalities in the protocol

In Daniela's descriptions of compliance as a change in eating patterns, there is an implicit critique of the protocol's portrayal of the problem of overweight and obesity. The care for patients is shadowed by the formal requirements of the clinical trial. This is a view shared by other staff. In nurse Ninni's words:

I think that many feel that the whole thing was very study oriented in a way... sometimes. You wanted very much to take good care of the patients when it suited the study... [...], but at the end of the study, it wasn't so... That was an issue that was often brought up, that "but in the end, what happens to the patient now?"

(Ninni 2004)

Here, Ninni shows how she thinks too much emphasis was put on the clinical trial, itself, at the cost of taking care of the participants.

Denise talks about the health care related problems implied in working with a more or less rigid research protocol. The kind of health care performed through the protocol practices is not always suited for each individual participant, something which concerns Denise. If she

had worked in the clinic, there would have been the possibility of suggesting a different treatment if the current one was not successful. This was not possible in a drug study where the participants must stay with the study and its particular treatment, even if it turns out not to be “the right thing” for some of them.

You can see that some are still there out of pure courtesy..., that they have undertaken to do this but that it really wasn't their thing, that it is not helping them or that it really wasn't that important to lose weight after all [...]. And then it doesn't always feel meaningful to just sit and make smalltalk each time.

(Denise)

This sense of some visits not being “meaningful” (Denise) and the concern about what happens to the participant after the study is over (Ninni) can be seen as indications that the rationality of the protocol clashes with the rationality of the care work involved in the staff-participant encounter. It also mirrors what Meuller (1997) has called the science/care dilemma (see also chapter one). According to the protocol, the participants were primarily research subjects. In the trial practice, as we have seen, they were very often also seen as patients. The staff was supposed to call them participants, and in talking to me they sometimes corrected themselves when they referred to the participants as patients. The constant switching between the terms participant and patient signals an oscillation at play between rationalities, not only in the basement discourse, but also in the protocol.

The two rationalities of care and the research inherent in the protocol may seem to exist side by side without much tension, as the oscillation described above between them signal. This is not wholly the case, however. Some parts of the staff consider the work to be too oriented towards research instead of care. When talking about the examining doctor's role in the Obe trials, Maria says:

It's important that the papers are filled in properly, but, since I meet them anyway and do the medical judgement... you are the patient's lawyer and doctor in the first room. But I'm not [...] responsible for some kind of enterprise, for how much funding that has to come in, or something like that. So I can liberate myself from things that can affect how you perceive of the job you're to do [...] Some of those visits are a challenge and can be interesting. But some, when you think about it, aren't as fun. It's not medically motivated to see someone again after say only two weeks.

(Maria)

Maria said that it was important both to fill in the forms and to make the medical judgment. But she stressed that the most important thing was “being the patient’s lawyer and doctor”. She also pointed to the fact that she did not need to account for “some kind of enterprise” and consider financial issues. Being free from such concerns made it possible to be there as a clinical doctor only, to focus solely on the patients’ needs. The two rationalities of being a clinical doctor and a research doctor are apparent here, as well as the way in which Maria negotiates her own position between the two.

One illustration of a tension between research and care can be seen in the event described by Martin. Staff on one occasion found the pills on trial in the toilet bowl, apparently a place where one participant, for whichever reasons, thought they belonged. The incident illustrates that some participants are motivated enough to stay in the trial for other reasons than the potential effects of the drug. They can be compliant towards the nurses and staff but noncompliant in terms of the protocol.

The incident is an example of a topic of conversation that sometimes occurred over coffe-breaks: what the participants’ reasons really were for coming to the visits in the first place.

I felt that it was some form of therapy, and it was crystallized pretty soon which ones would stay [...] because some of them were totally unmotivated, and you know that they didn’t take the pill but flushed it down the toilet, and the like.

(Martin)

For whatever reasons, participating in clinical trials was popular, as evidenced by the large number of people who called after the television commercial made by SpinOff and from the relatively low drop-out rate in the trial. According to the nurses, this was because the study took the participants’ eating habits and lifestyles seriously, something that the primary health care system was said to have failed in doing. Most importantly, though, is that this incident indicates that the participants were not passive research objects or victims, but able to act and make choices of their own. The throwing away of the pills in the toilet can be seen as an expression of the participant making use of the situation in a way he or she found most beneficial to his or her needs. They could stay in the trial due to loyalty towards staff or because they benefited from the care supplied, not because they believed the pill being tested was working for them or because they were interested in contributing to the scientific development of an obesity drug.

Interestingly, the work of motivating participants to change their lives to become healthier may be so successful that the participants even forget the reason why PharmaCo wants them there in the first place. This was illustrated by Nina when she spoke about what sometimes happened when the informed consent papers were signed. When informing participants about changes done in the study, which makes it necessary for them to sign a new informed consent form, she noticed that the information sometimes had not been fully understood by the participants.

You experience that all this with information does not ‘go in’, I think. Even if they have read and signed [...] it’s hard ... for them to understand what it is they [PharmaCo] are after. They can be like: “oh, is *that* what they’re looking at?” even if they’ve been with it for a while.

(Nina)

There is a tendency, according to Nina, for the participants to forget they are part of a research project. To some of them, it was not primarily the drug being tested that was the main reason for their participation. That they did not engage in the information provided about the trial signals that they trusted what was being done to them in the trial, something that can also be attributed to the work put in by staff in making participation feel meaningful by treating them as individual patients rather than standardized participants.

Mediating between research and care

In this chapter I have showed that nurses and dieticians do considerable amounts of work to make participants compliant – work that make the encounters meaningful for the participants and also for the staff. The job of the nurses in the Obe trials is often described by the trial’s designers as simply following the protocol and taking the required tests. Judging how to do this, however, requires knowledge about the participant’s conditions as well as experiences of treating other participants with the same problem. Most of the nurses and dieticians working with the trial have also worked upstairs and are part of a team involved in obesity care. The professional knowledge and experience needed for this work is used in the clinical trial, since many of the issues that come up in the clinical trial situation are not protocol-related. Such issues can range from concerns about diet and exercise to psychological problems and headaches. Therefore, parts of the nurses’ and dieticians’ skills consist of being able to make

the work prescribed work in practice, which is necessary because this work often is more complicated in practice than stated in instructions or guidelines.

As Oudshoorn has shown, this work is done through giving participants access to medical care and through creating a pleasant atmosphere. Making the participants continue with the Obe trial meant that the dieticians at times had to digress from the protocol instructions, and not hand out the designated standardized lesson. It also involved counselling the participants who brought up different types of personal problems. I have shown that the persons who do this work were primarily nurses and dieticians, the ones meeting the participants most regularly. This work implies that they have a very strategic position. It is they who are the ones that motivate and justify the protocol's requirements to the participants. Such a negotiating position between PharmaCo and the research subjects in the Obe trials can further be seen to imply the staff are mediators between "research" and "care". In a situation where those responsible for the drug trial as a whole often are not engaged in everyday clinical practices, such mediation falls on the shoulders of the nurses and dieticians.

The participants in the Obe trials are referred to both as patients or participants by all staff groups. This signals an ambivalence as to if the participants are research subjects or patients. This is an ambivalence sometimes mirrored in the participants' behaviour – they ignore the details of the study or stay in the study but do not take the pills. The participant-patients in the trial can be seen as "boundary objects" (Star and Griesemer 1989) that are both adaptable to different viewpoints (that of research and that of care) and robust enough to maintain identity across them. In relation to the rationality inherent in the protocol, they are research subjects, but in relation to the rationality inherent in the work of adjusting to and motivating the patients, they are patients with individual needs and specific concerns. The staff thus produce compliance towards both rationalities, but in a broader way than the protocol defines. Transforming the participants into patients is thus one major part of making the protocol work and one that seems to be successful.

Enacting different obesities

It is so important to see that obesity is a lot of different things. That some people are fat because they have a much too comfortable lifestyle and are totally unaware about how much they eat. Others eat for comfort, some out of grief and some out of happiness. These are different things, but it is all called obesity. [...] That's why obese patients need different treatments.

(Maria)

Social science research on medical practices and the body suggests that medical conditions are socially constructed. Studies of previously medicalised bodily states such as hysteria and homosexuality have shown how socially unaccepted desires or behaviours were dressed in a medical jargon and constructed as disease. Treatments and conditions have also been presented as co-constructed, meaning that not only does medicine construct disease, but that the disease or condition also defines what the treatment is (Willems 1998). Mol posits that, a condition or disease is not only about how it is represented, something that most constructivist studies focus on, but also about how it is “enacted” (2002: 55). She calls this a praxiographic appreciation of reality. It implies a turn from an epistemological appreciation that focuses on how each actor constructs a condition, to a praxiographic appreciation which focuses on what the condition *is* – not as it is ‘out there for all to see’, but as it is situated in heterogeneous practices involving persons, devices and discourse (Ibid: 53-54). Through a praxiographic appreciation, practice is privileged over knowledge in the analysis, or “doing” over “knowing”. It then becomes more important to examine how doctors, nurses and dieticians “do” obesity in the clinical trial through their diverse tools and practices than what they “know” about the condition.

In this chapter, I will describe how the overweight body and the weight loss pill are done or enacted in the Obe trials. Such a description will give a picture of what obesity is from the perspective of the nurses’, dieticians’ and doctors’ involved in the everyday work of the trials. Analysing my material this way, I will show that definitions of obesity and notions of what obesity is are clear-cut in some situations, but not in others. Thus, there are multiple definitions, enactments and notions of obesity at play. In her book on a cancer trial, Löwy has

similarly pointed to how those rare medical oncologists working with both patients and laboratory research had to deal with different frames of reference between the laboratory and the clinic, and how they adapted to a continuous oscillation between them (Löwy 1996: 247ff). The chapter starts off by discussing what can be said about how obesity is enacted by looking at the protocol's production tasks. Two contrary examples of how this was done are brought up: the situation where a CT is performed on the participant and the situation where the participant receives "non-pharmacological" treatment. The ways in which obesity is enacted in those two cases are then related to what the different staff groups say about obesity, what its causes are and how it, ideally, should be solved. I will show that these seemingly contradictory enactments all fit into the protocol, due to the coordination of beliefs and goals performed by the clinical trial staff.

Different drugs for different obesity

In a randomized controlled drug trial, the important thing from the perspective of the protocol is to evaluate how the substance affects the participants' bodies. The data defined as relevant for assessing the substance's efficacy is related to well-defined aspects of the biological body; body mass index, waist hip ratio, body weight, distributions of fat in the body. Aspects related to known concomitant conditions are also taken into account through the standardized measuring of insulin levels and blood pressure and of electrocardiogram (ECG) testing. Routine tests to measure tolerability of the drug are also done through laboratory testing of blood and urine samples. The pill's effect is both defined and measured in biomedical terms.

The premise for the Obe trials is the definition of obesity as above 30 BMI, a definition that is now widely used both inside and outside the medical arena. In order to participate in the Swedish trial, the participant has to be obese, i.e. above BMI 30, or above 27 if early onset diabetes is present. Obesity, according to the protocol, then, is a biologically and quantitatively defined disorder. Through the diverse production tasks described in the previous chapters, the trial nurses can be said to enact obesity as belonging to a body consisting of different quantifiable parts.

Such a body is also apparent in the protocol. It implies a body whose many characteristics can be measured, so that the effects of the drug can be monitored through the changes of these characteristics. The substance under testing, in line with such a view, is taken inside the body's boundaries and the body's reactions to this outside agent are measured.

All obesity drugs do not depart from the same exact description of obesity, however. In Willems' study of drugs against asthma, he challenges the presupposition that "asthma" and "lungs" are given entities. He does this through pointing to the differentiations that various drugs produce and that drugs are among the elements in a particular situation that "define (at least partly) what the other elements are" (Willems 1998: 109). The two different treatments for asthma that he studied build on different descriptions of the lungs' functions.

Similarly, the two obesity drugs that have passed clinical trials and reached the market in Sweden, underpin two different descriptions, or different aspects, of the condition that they are designed to relieve. It is important to note, however, that in the marketing of these drugs, it is emphasized how important it is to combine the drug with a healthy diet and exercise. In the case of Xenical, there is even a call centre funded by the pharmaceutical firm producing it that answers questions concerning diet and exercise and gives individualized advice on how to lose weight. For confidentiality reasons, Obe's biomedical characteristics will not be described here (see chapter four). Instead, the two drugs that have been registered for obesity; Xenical and Reductil¹⁴ will serve as an example to illustrate my argument.

The most widely used obesity pill, Xenical, works locally in the intestines through inhibiting the enzyme lipase that helps in the absorption of dietary fat. This leads the body to absorb less fat through the intestines. It can therefore be said to constitute obesity as an intestinal problem of fat uptake.

Reductil is not as widely prescribed as Xenical and builds on different underlying assumptions of what obesity is. It is a so called SSRI substance – selective serotonin re-uptake inhibitor – and belongs to the same family of drugs as certain anti-depressants. Reductil functions in that it affects areas of the brain that control hunger. Here, the problem of obesity is constructed as a one of feeling hungry.

Following Willem, one can see that these two different therapeutic practices treat, or enact, different "obesities". So, what obesity actually is becomes different depending on what drug, or treatment, is involved. The object – obesity – is not a stable one, as also indicated by the quotation from Maria introducing this chapter. Rather, obesity follows from the situations it is involved and enrolled in.

¹⁴ Reductil is similar to, but not exactly the same as the FDA approved drug Meridia in the USA.

Obesity enacted in the CT room

Participants in the Obe trials meet all kinds of monitoring devices, from carefully calibrated scales and measurement tapes, to echocardiograms, computer tomography (CT) and Dualenergy X-ray Absorbtiometry (DEXA). One can argue that through such kinds of monitoring practices, our awareness of our bodies is being amplified. Balsamo conceptualises such different types of devices as “visualization techniques” that fragment bodies into parts, “organs, fluids and ‘bodily states’” (Balsamo 1995: 216), affecting our views of the body and turning it towards a more “self-conscious self-surveillance whereby the body becomes an object of intense vigilance and control” (Ibid.). Thus, these technologies are not neutral technical devices, but have effects on our views of the body.

In the CT room the body is enacted as one which consists of organs, air and body fat: a biomedical body. CT scans were performed on the participants in the Obe trials four times according to the protocol. The character of the nurse-participant encounter in the CT room was different from the one in the basement. In the basement, as I have shown in the previous chapters, great care was taken to see to it that participants stayed motivated to return to the visits and the social contact with the participant was very important for this to be done. In the CT room the character of this relationship is different. It is more mechanical and less personal. A nurse welcomes the participant, explains what is going to happen, straps her to the CT scanner’s patient platform which is inserted into the machine, and makes sure the participant is comfortable. The straps are used to help to make sure the participant is still while the machine is running, a precondition for good quality pictures to be taken. Once the participant is in position, the nurse steps in behind a glass wall into what resembles a control room with displays, diverse levers and buttons, and waits for the pictures to be taken. An automatic voice then takes over the contact with the patient, telling the participant when to breathe:

Breathe in...breathe out...hold your breath [long pause] start breathing normally again.

During the pause where the participant holds her breath, five pictures are taken of five different sections of the body, in the way specified in the protocol. Air in the body is clearly visible in the pictures, which is why it is important to see that the participant has breathed out.

The CT scan is used to produce an image of where the fat is located in the body. The CT gives a more exact picture than other monitoring techniques, such as the less technologically

complex body mass index or waist hip ratio. The advantage of using the CT, is that it shows how much of the body fat is located inside or outside the bowel; an issue because fat located inside the bowel involves a greater medical risk than fat on the thighs or buttocks. The fat outside the bowel is, in medical terms, termed subcutant, while the fat inside is termed visceral. The visceral fat implies higher risks for coronary heart disease.

At the site of the Obe trials, images of this subcutant and visceral fat were hanging on the illuminated board on the wall next to the CT machine in the clinic. They were shown to colleagues from other hospitals or other interested guests to point to what the CT was used for, and as examples of the pictures made by the machine. Bodies with significant amounts of fat tissue are known as obstacles in radiology practice, since the fat causes blurry and therefore lower quality images.

The images were also used to show how the technology works with different types of bodies. “And here’s a picture of female and male fat”, I and another visitor were told when showed the CT room. The pictures showed the results of the scanning process and use the male versus female image as an example.

Research on the relationship between imaging technologies and bodies point to visual representations as being powerful instruments (Rapp 1997). The representations produced in the other parts of the trial, such as through written records in shape of case report forms, do not provide as powerful framings for what they portray as do the images.

It can be argued that the CT images contribute in shaping pictures of body fat in a gendered way. Images, more than merely showing how a CT works and the distribution of bodily fat, can be said to become visual representations of male and female bodies. This can be related to how of the doctors talked about the differences between the men and women who go to the clinic:

Men don’t put on weight the way women do. Men collect their fat inside the abdomen, and fat in the belly doesn’t just lie there like dead meat, it affects the metabolism.

(Mikael)

This representation of male and female body fat was given by one of the doctors I spoke with. It shows how, when a seemingly neutral image gets involved in discourse, the meanings of what the image portrays are flexible. Conceptions of female and male fat are introduced in to professional discourse, where they become attached to culturally stereotyped images of male

and female characteristics, something also demonstrated by Emily Martin's study of the prescribed characteristics of the egg and the sperm in medical textbooks. Martin's work shows that the way biologists describe what they discover is shaped by social imageries; the egg as a damsel in distress and the sperm as her rescuer (Martin 1991). Such use of social imagery to describe visual representations of the body then, conversely, easily becomes a fact which can provide "natural" explanations for social phenomena.

In the choice of pictures displayed in the CT room, biological and social differences between men and women are confirmed; there are broader cultural meanings to female fat as passive "dead meat" and male fat being active and "having an effect" on the body metabolism. The images (re)produce gendered meanings of the body as well as reinforce female and male stereotypes. These images then become visual facts that circulate in professional descriptions of obesity. Biological sex becomes located not only in the gametes (Martin 1991), the hormones (Oudshoorn 1994) or chromosomes and genes (Åsberg 2005), but also in the body's fat tissues.

In this way, as well, the "untypical" women who have beer bellies and the "untypical" men with big behinds are made invisible. This is not trivial. The co-construction of passive women and passive body fat, on the one hand, and active and dangerous male fat on the other, can have implications for what specific bodily conditions biomedicine focuses on and where funding for medical research is allocated. "Male" high risk obesity may be prioritised over the health needs of obese women who are perceived to be less at risk. This is so, even though obese women outnumber obese men, both as visitors to the clinic and as volunteers for participating in clinical trials.

Enacting obesity in "non pharmacologic therapy"

In most parts of the standard procedures in the protocol, such as the CT scan, obesity is enacted as a purely biological entity. The testing and use of pharmaceuticals for obesity implies a pragmatic view of the body as an organic and bounded entity separate from its "social" milieu. The dietary treatment of the dietician, the "non-pharmacological" therapy whose effects the drug is compared to, however, implies a different way of thinking about and dealing with obesity. When the participant enters the dietician's room, something she or he does at each and every visit, she or he sits down on a chair and talks to the dietician. This is the only station in the trial where the participant is not weighed or measured. Instead, the

dietician is interested in what the participant has done in terms of changing her or his eating and exercise patterns.

The dietician asks the participant about issues in his or her life that he or she thinks are important and affect the ways and what he or she eats. Participants may be very successful in keeping the diet they had been put on in a previous visit, but may fail to keep it when things in their everyday life turn difficult. This can lead them to fall back to previous eating patterns. How “non-medical” issues such as the participants’ family relationships and work life affect participants’ eating patterns, and thus body weight, come into focus in the dietary treatment part of the clinical trial. Relationships, eating patterns and work life are brought up in relation to the participants’ body weights. Thus, the body becomes situated in its social context.

The logic behind dietary treatment implies a different view on what the characteristics of obesity are. Inherent in the dietary treatment is a view of the body as part of the participant’s life as a whole. Treating the condition thus implies taking the participants’ whole life situation into consideration to find ways for the individual to make changes that he or she can stick to in the long run and that are adjusted to his or her individual preferences. In contrast to what is implied in the pharmacological treatment and the CT scan, obesity is here enacted as a social, behavioural or psychological problem that relates to the individual participant’s broader life situation.

Localization through coordination of beliefs

I have shown how obesity is enacted in different ways in the CT practice, biomedical tests and non-pharmacological treatments. I will now turn to local discursive practices on what obesity is, and why people become obese in order to understand how these relate to the previous enactments.

In the medical-scientific view of causes and effects of obesity (the ethiology of obesity), biomedical, social, psychological or genetic explanations are portrayed as complementary factors. Obesity is perceived as multi-factorial. Each medical-scientific account seems to add to the collective knowledge of the “whole truth” about obesity.

This is mirrored in how nurses, dieticians and doctors in the clinic talked about obese bodies and patients. Biomedical, scientific and clinical definitions of the fat body exist side by side with social, cultural and psychological ones, and even though the scientific medical definitions were pervasive in the basement, such ‘social/cultural’ images of fat people seeped through.

“Well, we have a measuring tape and a scale – but you can *see* if they are fat or not”, said one of the nurses I talked to during my fieldwork. This was said jokingly but it nevertheless signalled that the conceptions of a fat person in the clinical encounter were, at times, seen as primarily social/cultural. Fat could be defined without monitoring devices. The statement also conveys a sense that the intense measuring practices are of little help in the clinical encounter. Similarly, one of the doctors said that staff did not consider people having a body mass of 30 (above which one is categorized as obese) as sick. In fact, they are not even considered “that fat”.

Thus, sometimes staff gave biological descriptions and explanations for obesity with the help of biomedical scientific evidence and different monitoring techniques. At other times, obesity was conceptualized as a larger, structural or societal problem caused by increasing amounts of fast food restaurants and inactive lifestyles. Some of the extremely obese patients were thought to have severe psychological problems, while other patients, often people with low education levels and/or ethnic minorities, were perceived of as unaware of what good eating and exercise habits were.

Obesity as a psychological problem was also a recurring theme. One researching psychologist working with obesity in a different department said she thought it strange that the clinic did not offer its patients professional psychological therapy, considering that some of the patients had, in her opinion, severe eating disorders in line with anorexia or binge eating, and, according to one nurse, the patients considered severely obese, were almost always depressed. Another nurse mentioned theories about sexual childhood abuse as causing severe obesity in adulthood.

When dealing with obesity, staff thus put forward many different explanations and causes for the condition. Maria, who was quoted at the beginning of this chapter, later returned to the multi-faceted nature of obesity:

I think obesity is a lot of different things. It's not just about what you weigh. The more obese a patient is, the more complications there are [...] It's not just about having meals on a regular basis when you weigh 130 kilos.

(Maria)

To Maria, obesity was not one single measurable thing, and the complexity of reasons behind obesity increased the more obese a patient was. But a social or environment focused dietary

treatment did fully address obesity, either. For someone weighing 130 kilos, eating, exercise and behavioural advice was not enough.

You can work with obesity in different ways. You start with health education for those who are obese or pleasantly plump. But something very different is required when it comes to those who are really fat, because I think they have different diseases.

(Maria)

Maria here talks about obesity as being two different things. Educating those who are pleasantly plump was one way to treat an overweight patient, while treating those who are “really fat” demanded other types of treatments. The reason behind the “pleasant” obesity is the increasingly comfortable lifestyles that was often referred to. Remote controls, escalators, cell phones, and taking the car to work all contributed to the “pleasant” obesity, in combination with a plentiful supply of high energy foods in large portions.

Even though the biological body pervaded the protocol, all of the doctors I spoke with agreed to the description of obesity as, foremost a social problem. The explanation for “pleasant” obesity was in a stark contrast to the implicit ethiology of the drug therapy being tested in the Obe trials, where underlying explanations all had to do with appetite. When it came to “pleasant” obesity, the causes emanated from society, and terms such as “a disease of civilization” and “welfare sickness” were used.

However, reasons for being obese were not only located at the societal level. Clinicians also talked about individual behavioural reasons for being obese, especially when it came to the more complicated cases. These explanations ranged from characterisations of the condition as an eating disorder to descriptions of personality traits. Some patients were said to be “incapable of careing” about what they had to do in order to lose weight. Of others were said they suffered from a lack of knowledge or education, and inability to understand what was required of them. In the interviews, it was often mentioned that there was little correlation between what patients thought they ate and what they actually ate. Explaining that weight gain was the result of eating more than patients thought they ate, at times led to frustration for staff:

You show [them] that *you* think you eat this much, but you *really* eat this much. “Where do you get the rest of the calories from? You don’t get them from the air you breathe.” But you need some kind of intellectual sharpness in order to see the connection. And not all [of the participants/patients] have the education or ability [to understand that].

(Mikael)

The root cause of obesity is seen by staff as predominantly related to the participants’ way of eating. A dietician’s job is very complex and involves physical, social and psychological aspects of obesity. This is evident from how dietician Diana explained how she would work in a “regular” patient-dietician visit:

... one has to take care in asking careful questions about what these persons have with them, so to speak; why they have gained weight, for how long they’ve been overweight. Were they overweight as kids already, or perhaps after pregnancy or after they stopped doing sports, or became unemployed? Whatever it may be...to get a picture of how the weight problem became established and what stable weights they’ve had. Often people have certain weights where they have been relatively stable. And then I do an accurate nutritional analysis to see where the problem might lie, such as “I eat too much cheese” or “I drink too much soda”. It can be a lot of very different things. So you want to get a discussion going.

(Diana)

The excerpt shows how Diana considered a number of different aspects involved in a person’s weight problems. This was something that was quite contrary to the implicit view of the problem as formulated in the protocol, where the reasons as to why the participant is obese do not seem to matter. Her work included asking what “these persons have with them”, an expression stressing the individuality of each person and that each one had a different background and reason for gaining weight. For Diana, asking for what weight level had been the most stable in the participants’ lives was seen as important background information for giving informed advice. Diana would also do a nutritional analysis method used by dieticians to get a clear picture of the person’s eating patterns in terms of what they eat, as well as where, when and why they eat.

At times, staff expressed irritation over participants who, as in one case, claimed they “only ate salad”, but still kept gaining weight. The issue of being overweight or obese can awake certain feelings of irritation and a strong sense of not understanding the problem of obesity: why is it so hard to stop eating when overeating is known to be the reason for weight

gain? When talking to staff about participants' eating patterns, many ideas of what the patients' problems were brought up. In daily clinical practice, many ideas around why patients are overweight get formulated. One dietician focuses on the eating patterns of the patients in this excerpt:

[...] many of them have very messy eating patterns, and they vary a lot from day to day, they eat different things but there is neither rhyme nor reason to their eating schedule. And if there isn't, they can spend a whole day feeling as if they haven't eaten anything, not a single real meal. So when they finally start eating they notice how hungry they are and then they eat a lot. And then there are others who eat small things the whole day long and have no idea how much it adds up to in the end. So structuring the eating is an important thing.

(Daniela)

This quote has to do with persons who for one reason or another do not eat at regular times. There is an understanding among all staff groups that the reasons for becoming obese are complex. Coming to grips with what is psychological, social or biological is a difficult issue, as is the case with other health issues/diseases. This may be due to the widely mediated lay knowledge about obesity, mediated especially through evening papers and (mostly) women's magazines. Therefore, it is even more difficult to isolate obesity as a strictly medical problem, something that is perhaps easier to do when it comes to a disease such as cancer.

The feeling that patients did not understand that the excess amount of energy from eating too much ended up on their bodies, was a recurring theme among the staff who saw patients on a regular basis. The notion was constructed through their experiences with patients who accounted for what they had eaten since they met last time, in detail, but where the equation of energy intake and energy expenditure simply did not fit.

Since I have not interviewed participants, it is difficult to say how they viewed their condition. It is possible, however, that the participants enacted different bodies outside and inside the clinic. Cohn has analysed the role of dietary advice in his research on treatments for diabetes. The dietary advice is something that one patient in his study saw as corresponding to the diseased body, which is the body that she had already divorced from her own sense of self in the lived world outside of the clinic (Cohn 1997). In praxiographic terms, this patient enacted different bodies inside and outside of the clinic respectively. The enactment in the clinic involved a body that was not seen as part of her when she left the clinic. Hence, Cohn suggests that the body and food and disease were something that was perceived of differently

by the patient and dieticians, implying that the patient can embody disorder and fragmentation, and be unruly, while the dietary advice implies a view of the disease and person as integrated and, moreover, controlled by the individual. As the individual changes context, however, this sense of control may shift, too. In the situation in the clinic that I just described, seeing the connection between weight gain and what the participant eats may be clear to patients during the appointment, where patients may feel that they are in control over what they eat. Once they are back in their everyday life, however, they may lose that sense of competence and control.

That obesity is enacted differently in the clinic also has broader social consequences. It can be argued that it affects where blame for obesity is directed. When it comes to pharmacotherapy, the blame is put on bodily processes that the obese person cannot control him or herself. This can be a relief to many obese participants, since it frees them from feelings of guilt and society's usual way of portraying obese people as lazy and unable to restrain or control themselves. Emphasizing the social has the opposite effect, where it becomes the participant him or herself that is to blame for having an unhealthy lifestyle. The weight issue becomes individualised and the participant is made aware of the problems they may have in life in general and how they are related to their more or less excessive eating. Thus, participants are given an ambivalent message as to whether the health care system can help them or if they have to help themselves.

The different ways of talking about obesity that I have presented here can be seen as yet other ways in which obesity is being enacted discursively. But, to return to Willems and the co-construction of treatments and its conditions: where does a weight loss pill, with which the body is enacted as a bounded, integrated and controlled entity, fit into the clinical discursive enactment described above which implies a different body that is socially and psychologically situated? In talking to Denise, it seems that it does not fit so well:

It's probably great for some people to use a drug as an extra help. But you still have to be prepared to make lifestyle changes.

(Denise)

Denise points out that one needs to be prepared and willing to make changes in lifestyle. Thus, Denise sees the pill's function primarily as a way to give incitement to the patients to continue the laborious work of changing their lifestyles to a healthier diet and exercise. The

drug in the dietician's office is therefore enacted as a tool for elevating the participant's motivation, rather than a tool for losing body mass.

This contradiction between the pill increasing patients' motivations to change their lifestyles, on the one hand, and lessening the patients' appetites through biomedical means, on the other, is also mirrored in the dieticians' and doctors' talk about the pills. In Disa's words:

I don't think we can help our patients by surgery and pills, primarily. But maybe that is what we have to do today because there isn't anything else [to do]. But I think that you have to attack this on a societal level.

(Disa)

So, from that perspective, what do you think about the extent to which drugs are being developed?

(Petra)

Well... then, negatively, really. But at the same time, I'm being realistic. I see it as utopic that we would be able to help people in the way they would want [...] I also see patients who can't handle their situation, who have this urge towards food and sweets and what have you. They can't handle it and long for finding a way to be able to. And, of course, if you can find a drug that can help you a bit on the way...and without side effects.. that wouldn't be all wrong. It wouldn't. Because society is the way it is.

(Disa)

The view of obesity pills here is a pragmatic one where the pills are one possible solution to a problem that really should be tackled on a different level. The role of medicine in such a case is, as Mikael pragmatically put it, to "bandage up the extreme cases a little bit". Trying to make sense of the extensive drug development in a scenario where obesity is seen as foremost a social and psychological problem which there is not much one can do to help, can be seen as a work task in itself. It is a kind of work that involves coordinating the beliefs about the causes of obesity, on the one hand, and the goals of clinical trials, on the other. It involves making sense of why pills for a biomedical body are tested on a condition whose causes are not seen as biomedical, but social and psychological.

This work of coordinating beliefs and goals thus connects to the focus on articulation work in the previous two chapters. It is yet another aspect of the articulation work needed for the protocol to be localized into the everyday setting.

Incorporation of multiple beliefs and goals in the protocol

This chapter has shown that multiple beliefs about what obesity is and how it should be treated are enacted in the practices of the trial. A patient's social situation, individual psychology and broader social issues seem to be what dieticians, nurses and doctors consider lie behind most forms of obesity. Despite this, the treatments being tested are predominantly drug therapies where obesity is measured mostly in purely biomedical terms.

In Marks' historical case of a "diet-heart study", he argues that the support for the drug studies "represents the medical profession's preference for drugs over diets and treatment over prevention" (Marks 1997: 192). But such an argument does not take the differences *within* the medical profession into account, where those involved in clinical trials are more prone to embrace them than those who are not. Neither does the argument take into account that the advocates of drug therapies may not necessarily believe they are the *best* solution to the problem. This was evident in how staff talked about obesity in the clinic.

Drug therapies and non-drug therapies against obesity do not compete on an equal basis. The power of the pharmaceutical industry and the status of randomized controlled trials, RCT's, in relation to other methods of evaluation makes it difficult for non-pharmacological research to be performed. It is more difficult to receive funding for non-pharmacological research, and RCT's the size of the Obe trials cannot be performed without private sponsorship. The alleged "low evidence strength" of non-RCT ways of evaluating therapies is an additional problem when it comes to obtaining scientific credibility for non-pharmacological therapies. The methods for evaluating dietary treatment are difficult to quantify due to difficulties in accurately measuring what people eat, which one of the dieticians brought up. Moreover, qualitative analyses do not fit well within dominant biomedical research paradigms. The problem of measuring dietary treatments is well acknowledged in the obesity clinic. "How can we be doing something when there is no proof of there being any effect?" was a question posed by one doctor after a staff meeting we attended. This quote reflects the role that the principles and methods of randomised controlled trials play in the clinic and the difficulties involved in introducing other methods of evaluation.

As I have shown, what obesity is differs within the Obe trials, where different obesities are enacted in the different situations. In the dietary treatment part of the trial, for instance, obesity is enacted as a social, psychological and societal problem, while in the drug therapy it

is enacted as a biomedical condition. Also, the role of the pill in helping patients lose weight is given two different interpretations in the clinic. In the drug trial, on the one hand, it is how the substance affects the participants' bodies that is important. This is reflected in the great number of measurements entered into the protocol, the tests taken, the CT and DEXA scans. The protocol focuses on aspects related to bodily functions, such as the effect the substance has on body weight, be it total body weight, or abdominal fat, levels of insulin, or blood pressure, and even psychological well-being. In the non-pharmacological treatment part of the trial, on the other hand, the bodies are seen as primarily affected by their social context. The role of the pill in this treatment situation is only to encourage and stimulate the participant to start taking steps to change his or her habits of exercise and diet. The pill's main function, here, is social, not biological or pharmaceutical. It may be seen as a lifestyle-changing pill for a social body.

In the trials, then, there are several different and seemingly incompatible enactments going on. The clinical trials succeed, however, in incorporating these differences within its design, thanks to the work put in by staff to localize the protocol. A support for drug studies, therefore, does not necessarily imply that different medical professions prefer drugs over other treatments or over prevention. Drugs are, rather, seen as a possible solution to a problem that really does not have an effective and safe treatment. So, under the circumstances, where the pharmaceutical industry sees a good business in developing obesity drugs, the testing of drugs signals a hope for those in need of a solution. However, it does not stop the different and competing enactments of obesity from taking place. Different obesities continue to be enacted, just as drug testing continues.

Testing pills, enacting obesity

In this dissertation, I have provided a description of the people and tools involved at one site where two large scale and multi-sited clinical trials were performed. This final chapter reviews my understanding of the work that was done in order to localize these tools. I will then discuss what the case study suggests about two particular issues brought up in the introductory chapter, namely the science/care dilemma in clinical trials and how a clinical trial participates in the medicalisation of a condition like obesity.

The work of localizing tools in a clinical trial

I have focussed on tools and work in a clinical trial and have thus emphasized its material, everyday and seemingly prosaic aspects. Such a focus may seem contrary to the image of the pharmaceutical industry as filled with hope, drama and controversy that is depicted in the popular press and in society at large. Underneath the seemingly commonplace façade of clinical trial work, however, and with some sociological imagination, there are dilemmas and contradictions along with hopeful expectations of a simple drug-based solution to a complex problem.

This study's contribution to previous research within the field of science, technology and medicine is twofold. First, it presents a new and unique case study concerning the diverse and multiple technoscientific tools and practices involved in one large scale and industry sponsored multi-sited clinical trial. At Centre University Hospital, where I did my observations, two different trials of the same substance ("Obe") but with slightly different research questions were performed: one Swedish, and one international trial. They were conducted at 20 and 40 clinics, respectively and simultaneously.

Marc Berg has shown how tools used to rationalize medical work both discipline the practice, but also need to be localized to fit into local practice. My theoretical contribution lies in showing how this localization is done through different kinds of visible and invisible

articulation work (Fujimura 1987, Star 1991b, Hampson & Junor 2005) on different analytical levels.

The dissertation focuses two central tools involved in conducting the Obe trials: a clinical research protocol and a computer control system. A clinical research protocol is a set of highly standardized, detailed and elaborate instructions that make the conducting of large scale multi-sited trials possible. A protocol reduces a complex reality into a predictable one open for intervention, something that needs to be done for it to be useful (Berg 1997: 153). The protocol studied here is an extensive document consisting of eighty-five pages. The very size of the trial and protocol makes it difficult to manage in a way that does not threaten the reliable production of data. All the details in these eighty-five pages need to be done in the same manner at all participating sites. The management of this endeavour was performed by staff in the clinic together with the pharmaceutical company monitor in the international trial, whereas it was outsourced to a private company in the Swedish trial.

Management of clinical trials has become a business niche of its own, and the work of managing clinical trials in effective ways is increasingly being outsourced to auxiliary firms, often referred to as contract research organizations, CRO's. One such company is involved in the Swedish Obe trial in focus in this dissertation. This company, SpinOff, develops software that is used in recruiting participants to trials and also centrally scheduling the different work tasks that the protocol ascribes to be done. Their patented computer control system is the second tool analysed in this dissertation.

The clinical trials are not conducted in a socioeconomic vacuum, however. They are conducted by pharmaceutical companies under increasing pressure and competition. Such a contextualization was provided in chapter two and necessary to understand the extent to which the clinical trial work processes need to become more effective. Moreover, and important to mention in this particular case study, the trials are conducted in a culture of intense preoccupations with thinness and dieting. This also had consequences for the efficiency in recruiting participants.

I have analysed these tools as they were used in the everyday work tasks of the clinic. In total, I spent three months at the clinic interviewing and observing trial nurses, doctors, and dieticians who were involved in the two different Obe trials at Centre University Hospital. The observations and interviews also included staff who worked at the obesity department and clinic in other projects. Interviews and observations alone did not help me to understand what and why specific tasks were done, however. I also studied the clinical research protocol which largely structured what was done. I also regularly consulted two handbooks in clinical trials

(Lemne 1991/1997; Jadad 1998) in order to make sense of what clinical trials were and the role played in them by the clinical research protocol. Thus, it became the relationship between what the staff did and how they understood what they did, on the one hand, and what actions the protocol prescribed, on the other, which became the focus in this book. Or, in Berg's terms, how the protocol both disciplined what was done but also how it was localized at Centre University Hospital.

I have described this localization process by distinguishing between different types of work tasks. The first distinction used is one between production tasks and articulation work (Fujimura 1987: 258). Production tasks are those that are relatively clearly defined and thus, routine, such as the multitude of tasks that the clinical research protocol prescribes staff to do. I have shown how these production tasks include such diverse work as taking blood pressure, measuring waist-hip ratio, registering the side effects of the study drug, handing out dietary advice material and making telephone calls reminding participants when they are due for their next visit, to name just a few of the many tasks mentioned in the protocol. In describing how all these tasks were performed and how the work was organized and planned I emphasized the similarities between this work and assembly line production. In line with such a description, the protocol and computer control system were seen as objects that disciplined practice, something that also resonated in the way staff talk about the work in terms of "being controlled" and "working on the floor". The work of coordinating, planning and organizing the diverse production tasks is one visible form of articulation work that I grouped together as "classical management work" (Hampson & Junor 2005). Such work included tasks such as making templates for what was to be done at what point in time, and seeing to it that all necessary equipment and staff were in place to allow for a smooth flow of the work process. I showed how this type of work was done to a different extent in the Swedish and the international trial, respectively. In the Swedish trial this was managed by SpinOff.

The work that SpinOff did in the Swedish trial only involved the first type of articulation work, the visible traditional managerial work. SpinOff shortened the production process, mainly by its efficient participant recruitment methods described in chapter six, but also through a minute scheduling of the tasks that were to be done. This scheduling, organizing and managing of the production tasks was, in the international trial, performed by the clinic and the pharmaceutical company together. In terms of traditional managerial work, then, SpinOff took over the scheduling and organizing that had previously been done by the clinic itself. These tasks were thereby computerized and relocated from the clinic to a private company. Such a scenario points to what Mirowski & Van Horn recently claimed may be a

signal that an extraordinary replacement of academic health clinics in favour of CRO's is underway, something that has not been researched (Mirowski & Van Horn 2005: 506). Interestingly, when I returned to my field in 2004, to conduct a second round of interviews, I was told the number of staff had decreased drastically since the time of my observations as a result of SpinOff taking over the management of not only the Swedish Obe trial, but also subsequent ones. Due to pharmaceutical companies' efforts to cut costs for research and development, the need for efficient management of the trials is increasing. The increasing number of contract research organizations, CRO's, can be seen in this light.

I also showed that there are other, less evident, forms of articulation work involved in localizing the protocol in the Obe trials. In chapters nine and ten, the articulation work involved is of a different and more invisible kind. Chapter nine brought up what I assert is compliance work, or work done in order for the participants to continue participating in the trial; to stay "compliant". This included work where staff counselled and encouraged participants and at times even digressed from the protocol in order to motivate them to stay on in the study. Compliance work involved including "the patient" into the work, that is to say, a participant with non-standard and to a certain extent unforeseeable needs and characteristics. I showed that this work was done not only to make participation more meaningful for the participants but also to make the job more meaningful to staff. This compliance work shows that those nurses, dieticians and doctors involved in the everyday follow-through of the trial have a strategic position in mediating between the pharmaceutical company and the participants who constitute their potential market for the drug under study.

Finally, in chapter ten, I turned to the condition the drug was tested for, namely obesity. I showed the diverse ways in which obesity was enacted in the trial. In most production tasks performed, obesity was enacted as a measurable biomedical condition. In others, such as the dietary treatment tasks, however, obesity was enacted as a social and psychological problem where the participant's whole life situation was accounted for. This later view also emerged in interviews and conversations with all staff groups: obesity was discursively enacted as foremost a social problem, and as a psychological one in the more severe cases. Making sense of these somewhat contradictory enactments occasioned by the protocol requires a third type of articulation work that I referred to as coordination of beliefs about what obesity is. Altogether, these different forms of production tasks and articulation work were needed to localize the protocol and thereby make the trial doable, and to produce reliable data as efficiently as possible.

I have shown that the protocol disciplines practice, but also that staff do different things to localize the protocol and make the job doable. This is not a one-directional process where the protocol has effects on practice. Berg talks about a convergence of tools and practice where the tools discipline practice, but only to a certain extent. In a longer time perspective practice also shapes the tool in that there are continuous adjustments made to the tool as problems in its use see the day.

What makes my account of localization different from Berg's is a conception of the tool as disciplining the work to a higher degree than do the protocols he describes. The tool is not a heterogeneous actor on the same level as trial personnel; the tools and practices cannot "converge" in a symmetrical manner. The staff working with the trials can only change or affect the tool to a certain extent and only if the suggested changes fit with the goals of the protocol's designers.

Such a difference of interpretation also derives from my focus on the different practices involved in localizing the protocol, where I include more invisible work and especially the work done by those "on the floor". The staff did not necessarily see the protocol as a neutral tool, something illustrated by the way one of the nurses oscillated between the pronouns "it" and "they" when she talked about it. To her, the protocol represented a body of people whom she and others conceive of as controlling their work. This must be linked to the fact that the pharmaceutical clinical trial studied here is part of a long industrial production process, whereas the localization studied by Berg concerned protocols used for decision support to shape the patient's trajectory. The goals of producing a drug and helping a patient do not always converge. This is perhaps especially so in the kind of protocol studied here, one used in a trial where a pill is tested on people who are not actually patients, but could rather be categorized as people with elevated risk. So, rather than only being something that shapes the patient's trajectory, the protocol is used to shape the work process in the production of reliable data.

Ironically, then, my study is one of the localization of a clinical research protocol into a clinical trial practice where the trial participants are not considered clinically ill. Hence, the tools discussed here are not used to make medical work more efficient, but are primarily used to rationalize an industrial production process in the very competitive pharmaceutical industry. Rationalizing clinical trial work is thus different from rationalizing medical work in the absence of such a competitive environment. Seen in such a light, the protocol is more similar to the rationalization of work in e.g. a car factory. It has as much to do with efforts to make the production process quicker and control the workers so that they keep performing

their tasks with a maintained quality, as it has to do with the production of reliable scientific data. This protocol then, disciplines work more than in Berg's case where control is seen to be distributed across different actors.

Blurred boundaries

The major aim of this study has been to understand the tools and practices of everyday clinical trial work, with an emphasis on invisible work (Smith 1988; Shapin 1989, Star 1991a). In the introductory chapter I also outlined two further aims; to understand the science/care dilemma as expressed in the trials, and to understand the role of the clinical trial in the medicalisation of the condition of obesity. I will now briefly discuss what my case study has to say about these issues.

The protocol may appear to be a tool that is strictly rational and technical, but it does incorporate the contingent/experiential by leaving some production tasks more open and less standardized. The non-standardized part of the dietary treatment is one example of such a task, and the doctor's examination is another. The protocol can also be seen to encompass contingent and experiential aspects of the work situation through the work done to localize it. However, this does not necessarily have to mean it silences the experiential and contingent aspects of clinical trial practices.

Evidence based medicine contains the contradictory rationalities of the rational/technical (science), on the one hand, and the contingent/experiential (care), on the other (Pope 2003: 278). Pope sees the former as being privileged over the other. As shown in this study of the Obe trials, her conclusions do not apply to all staff categories or in all situations. For example, doctors involved in the non-clinical aspects of planning and designing of a clinical trial may privilege the former over the latter, while clinical doctors do not. Staff in the clinic are more focussed on the care aspects but they also continuously mediate between care and research, seemingly without problem. This is something that has also been pointed out by Löwy in her study of cancer trials, where the rare medical oncologist working with both patients and laboratory research had to deal with different frames of reference between the laboratory and the clinic, and how he adapted to oscillating between them regularly (Löwy 1996: 247ff). The situation of the trial nurses, trial doctors and dieticians in the basement can be compared to the shifting between different frames of reference by the medical oncologist in Löwy's study. They are the ones who are confronted by these different rationalities on an everyday basis:

seeing to it that the individual participants' needs are kept to, while at the same time following the instructions of a rigid protocol.

These observations indicate there is less of a conflict between research and care than often emphasized in the literature. I would argue that the boundaries between these are blurred in everyday practices in the clinic. This blurring of boundaries is expressed in the practices and interpretations of the Obe trials in two different ways: in the terminology used to describe the participants, and in the methods used to recruit patients.

First, I found it interesting to note that the category used to depict the persons involved in the trials was not a consistent one. The staff was supposed to call them participants, but they constantly slipped and called them patients instead. The participants were said to be receiving "care in the form of research", something also indicating a blurry border between care and research. Moreover, the text in the protocol referred to patients and participants in a haphazard manner throughout the document, as well. There was not only a blurring of the categories participant and patient, however. When discussing the role of rigorous safety standards in clinical trials, one of the doctors referred to there being other than patient aspects being accounted for in these standards, and in passing referred to the participants as consumers. In the everyday practices of the clinical trial, however, this terminology was not used, even though similarities can be seen between the compliance work performed and the work of claims processors as described by Wenger and the work of interactive customer service work as shown by Hampson and Junor (2005). These types of work can be seen to involve the same contradictory requirements of both pleasing the customer (i.e. compliance work) and staying in control of the situation in a way that fulfils the employer's goals of a quick and cost-efficient work process.

This brings us to the second example of blurry boundaries which concerns the methods used in the Obe trials for recruiting participants. These were seen as part of the scientific process from a medical research point of view, but as computer software development from the point of view of the pharmaceutical industry. The medical researchers who took part in the starting up of SpinOff saw the recruitment methods used as an important part of the research process; they were methods for recruiting *research subjects*. The methods were described in scientific articles, entered into the research doctors' CV's and publication records. Working with recruitment methods was thus seen as a medical scientific practice from their perspective. On the other hand, the recruitment system was seen as software development by the pharmaceutical firm involved in the trials. The firm was offered a share in SpinOff as compensation for their financing of the several "man-years" involved in programming the

system. However, the firm was not interested, since, it claimed it was not a software firm. To the pharmaceutical company, SpinOff did not deal with research, but rather with the management of a production process.

Thus, the tools and work involved in the obesity drug trial show how the boundaries between being a patient, a participant in a research project and a consumer seem blurry and being under reconfiguration. This does not mean, however, that the science/care dilemma has dissolved. Some parts of staff expressed concerns about the dominant position of pharmaceutical research at the clinic. Although the patient-participants have not been interviewed, my data does indicate that the boundaries do not seem as blurry to them, due to the compliance work performed by the staff. It would seem as if the work of making them compliant involves obscuring the science/care dilemma.

Medicalising obesity?

But, and returning to the final question addressed in this dissertation; what does all this tell us about the condition that the drug on trial seeks to treat? How is obesity enacted in these clinical practices? I would like to discuss this in two ways, the first linked to the kind of treatment given and the second to the recruitment process used.

The form of treatment given to overweight people mirrors where blame on the condition is placed. Is the individual to be blamed for his or her over consumption of food due to a lazy attitude? Is it state actors' fault for not stopping the increasing spread of "bad" food habits, or is it the multinational food industry that is the cause of the epidemic? Or is it all in our genes? As discussed in the introductory chapter, medicalising a bodily condition implies a focus on the genetic or physiological causes and solutions of the problem. The focus on pharmaceutical research to solve the problem of obesity thus implies a neglect of the socio-political issues around obesity. The practices of a clinical trial may therefore contribute to a depoliticisation of the obesity problem, in that taking a pill can legitimate the view that participants have an individual medical problem rather than a behavioural or social one.

As I discuss in chapter ten, the different practices involved in the clinical trial give a more multifaceted picture. Most production tasks depicted in the protocol are based on a view of obesity as a physiological condition outside the participants/patients' control. The focus on advice towards healthier lifestyles, evident in the dieticians' work, on the other hand, is not one of a medicalisation process. Dieticians' dietary advice could rather be seen as part of a

process of “healthicisation”, a term used by Conrad (1992). Whereas medicalisation suggests biomedical reasons and interventions for a condition or disease, healthicisation suggests lifestyle and behavioural reasons and interventions. Medicalisation implies that medicine stands for the moral, while healthicisation makes health a moral issue for the individual.

Obesity in the Obe trials is described in both ways. It is said to be a multi factor disease with social, psychological as well as biological causes. Where you have grown up, your ethnic background as well as your class and gender related life patterns can cause obesity, as can biological factors such as genetic predisposition. What can be emphasized here is that different practices contribute to medicalisation and healthicisation, respectively. Practices such as prescribing medication and interventions such as surgery both contribute to a process of medicalisation. On the other hand, the practises of the dietary treatment performed in the Obe trials, as well as the compliance work involved in localizing the protocol, can be seen (mostly, at least) as part of a healthicisation process since these practices situate the participants in his or her social situation, and consider behaviours and lifestyles as causes of the problem.

Given this multi-factor enactment of obesity in the everyday clinical trial practices, it is not surprising that doctors spoke about there being different obesities. This was described in other ways, as well. In particular, a distinction was made between those who were “pleasantly plump” and those with severe obesity and serious health problems. It is important to remember that the Obe trial participants did not necessarily belong to the later category, with serious problems, due to very narrow inclusion criteria in the protocol. Therefore, the staff often depicted the participants as not “really” being sick, or even as “not being that fat”. In fact, at least a proportion of those who were included in the trial belonged to a category that may not even have received a referral to the clinic, where only people with serious conditions were treated. The number of people coming into question for drug treatment thus exceeds the number of patients involved in obesity treatments in the clinic.

Following a similar line of argument, it can be said that the recruitment process of SpinOff not only speeded up the recruitment of trial participants, but also contributed to the exposure of obese patients and patients with early onset type 2 diabetes to the health care system. As another doctor said, many of these persons would not even have contacted the health care system for their condition had it not been for the heavy advertisement to find participants for the drug study. It was argued by yet another doctor that while it is good for overweight persons to be diagnosed early, since it could help motivate them to change unhealthy lifestyles, there may be other drawbacks involved. The health care system may

have to make reforms to accommodate the obese but healthy as part of its jurisdiction. One could argue that if the health care system already had the financial and other resources for such kinds of programs, people at risk may not have come as participants in the trial in the first place. The recruitment process in SpinOff has thus created a huge number of diagnosed people – but only 541 of them were given the possibility to participate in the study. A proportion of the ones who were excluded were left with a diagnosis, which they could either choose not to do anything further about, or choose to contact the public health care system. The latter options would result in an increased pressure on the public health care system. In addition, the recruitment process made them into a large potential group of consumers of a future drug to help them better counter the risks of obesity and an unhealthy lifestyle

The number of people who constitute the potential market for the obesity drugs may therefore have increased and the computerized forms of recruiting participants can be seen as a tool that expanded the market for obesity drugs. Such an expansion of the market also benefits the future development of obesity and diabetes research. The technical system and recruitment process also made available a large databank of overweight and obese individuals that could be used in further research. The database enables quick recruitment of participants for trials where similar volunteers are needed. SpinOff plays a central role in this (expanding) network of research, care and industry around this bodily condition. SpinOff's database of 80,000 willing trial participants is important for making such an obesity research networks possible and strong. In a situation where boundaries are blurred between the patient, participant and consumer, expanding the market might consequently mean an expansion in the areas of care and research as well.

The large-scale production of potential research subjects may also lead to new disease identities. From what dieticians and nurses state in the Obe trials, it can be said that patients seek help, not primarily in order to be free from disease or risk, but rather to lose weight for aesthetical or social purposes. What the participants encounter once enrolled in the trial, however, is a large variety of tests that will probably increase their awareness of the medical health risks involved in being overweight. In this way, it is also the desire to be thin – a common enough preoccupation in our society – that is medicalised.

Medicalisation is a complex process taking place on more and different levels than simply in the practices and tools involved in one drug trial, however. Further research needs to be done to analyse how patient identities are shaped through participation in pharmaceutical research and how this, in turn, affects the production of drugs around the patient's, participant's or consumer's condition.

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Interviews

The interviews were taped and transcribed.

Diana, dietician in the Swedish Obe trial, 26 March, 2002
Denise, dietician in the international Obe trial, 3 June, 2002
Daniela, dietician, 18 June, 2002
Disa, dietician, 18 June, 2002
Natalie, radiology nurse, 8 April, 2002
Nadia, trial nurse other drug study, 24 April, 2002
Nancy, nurse and administrative boss, 22 May, 2002 and 25 October 2004
Ninni, trial nurse in the international Obe trial, 11 April, 2002, and 29 October 2004
Nicole, biomedical analyst, 25 October 2004
Nina, nurse, 25 October 2004
Calle, computer engineer, 19 June, 2002
Maria, medical doctor, 23 April, 2002
Mikael, medical doctor, 10 April, 2002
Mats, medical doctor, 23 May, 2002
Martin, medical doctor, 4 November 2004
Magnus, medical doctor and principal investigator, The Swedish Obe trial,
25 November, 2004
Markus, medical doctor and professor, 24 November, 2004

Not transcribed but taped interviews:

Monitor at PharmaCo involved in the international trial
Research coordinator at PharmaCo responsible for the Obe trials in Sweden
Head of *Överviktigas riksförbund*

References

- Abraham, John (1995) The production and reception of scientific papers in the academic-industrial complex: the clinical evaluation of a new medicine. *The British Journal of Sociology*, Vol. 46, No. 2.
- Abraham, John & Reed, Tim (2003) Reshaping the carcinogenic risk assessment of medicines: international harmonisation for drug safety, industry/regulator efficiency or both? *Social Science & Medicine*, Vol. 57 No. 2.
- Adams, Vincanne (2002) Randomized Controlled Crime: Postcolonial Sciences in Alternative Medicine Research. *Social Studies of Science* Vol. 32, No. 5-6.
- Agar, Michael H. (1980) *The Professional Stranger: An Informal Introduction to Ethnography*. San Diego: Academic Press.
- Astrup, Arne (1998) Energibalans i Andersen T, Rissanen A & Rössner S (eds.) *Fetma/fedme – en nordisk lärobok*. Studentlitteratur.
- Atkinson, Paul & Coffey, Amanda (2001). Analysing Documentary Realities in Bryman, Alan (Ed.) *Ethnography (Volume III)*. London, Thousand Oaks & New Delhi: Sage Publications.
- Balsamo, Anne (1995) *Technologies of the Gendered Body: Reading Cyborg Women*. Durham: Duke University Press.
- Barry, Andrew (2001) *Political Machines: Governing a Technological Society*. The Athlone Press: London and New York.
- Benner, Patricia (1984) *From Novice to Expert: Excellence and Power in Clinical Nursing Practice*. Meno Park, California: Addison-Wesley.
- Berg, Marc (1996) Working with protocols: a sociological view. *The Netherlands Journal of Medicine* No. 49.
- (1997) *Rationalizing medical work. Decision support techniques and medical practices*. Cambridge, MA: MIT Press.
- Berg & Timmermans (2003) The practice of medical technology. *Sociology of Health and Illness*. Vol. 25, Silver Anniversary Issue.
- Berg, Marc & Mol, Anne-Marie (1998) *Differences in Medicine: unravelling practices, techniques, and bodies*. Durham and London: Duke University Press.
- Bergenheim, Klas (2000) *Essays on Pharmaceutical R&D*. Lund Economic Studies no. 88.
- Berner, Boel (1999) *Perpetuum Mobile? Teknikens utmaningar och historiens gång*. Lund: Arkiv förlag.
- (2004) *Ifrågasättanden: Forskning om genus, teknik och naturvetenskap*. Linköping: Tema teknik och social förändring, report No. 42.

- (2005) Problemen med problemet. Eller: Att fånga en Heffaklump, in Lundqvist, Åsa, Davies, Karen & Mulinari, Diana (eds.), *Att utmana vetandets gränser*. Malmö: Liber.
- Bordo, Susan (1993) *Unbearable Weight: Feminism, Western Culture and the Body*. Berkeley and Los Angeles: University of California Press.
- Bouchard, Claude et al. (1990) The Response to Long-term Overfeeding in Identical Twins. *New England Journal of Medicine* 322:1477-82.
- Bowden, Peta (1997) *Caring: Gender-sensitive ethics*. London and New York: Routledge.
- Bowker, Geoffrey C. and Star, Susan Leigh (1999). *Sorting Things Out: Classification and its consequences*. London and Cambridge: The MIT Press.
- Brown, Richard K (1992) *Understanding Industrial Organizations: Theoretical Perspectives in Industrial Sociology*. London and New York: Routledge.
- Bruch, Hilde (1978) *The Golden Cage: the enigma of anorexia nervosa*. Harvard University Press.
- Brunsson, Nils & Jacobsson, Bengt (1998) *Standardisering*. Nerenius & Santérus förlag.
- Casey, Catherine (1995) *Work, Self and Society: After Industrialism*. London and New York: Routledge.
- Clarke, A. and J. H. Fujimura (1992) *The Right tools for the job: at work in twentieth-century life sciences*. Princeton, N.J., Princeton University Press.
- Clarke A, Fishman J, Fosket J, Mamo, L & Shim J (2000) Technoscience and the New Biomedicalization: Western Roots, Global Rhizomes. *Sciences Sociales et Santé*, Vol. 18, No. 2.
- Chernin, Kim (1985/1994) *The Hungry Self: Women, Eating and Identity*. New York: Harper Perennial
- Cockburn, Cynthia (1983) *Brothers: Male dominance and technical change*. London: Pluto Press.
- Cohn, Simon (1997) Being told what to eat: conversations in a Diabetes Day Centre in Caplan, Pat (Ed.) *Food, Health and Identity*. New Fetter Lane, London: Routledge.
- Conrad, P. (1992) Medicalization and social control. *Annual Review of Sociology*, Vol. 18.
- Conrad, Peter & Schneider, Joseph W. (1980/1992) *Deviance and Medicalization: From Badness to Sickness*. Temple University Press.
- Cronje, Ruth & Fullan, Amanda (2003) Evidence-based medicine: toward a new definition of 'rational' medicine, in *health: An Interdisciplinary Journal for the Social Study of Health, Illness and Medicine*, Vol 7(3): 353-369.
- Doyal, Lesley (1979) *The Political Economy of Health*. Pluto Press.
- Ekelund, Mats (2001) *Competition and Innovation in the Swedish Pharmaceutical Industry*. Stockholm School of Economics. ISBN NR 91-7258-559-5.
- Eliasson M, Lindahl B, Lundberg V, Stegmayr B (2002) No increase in the prevalence of known diabetes between 1986 and 1999 in subjects 25-64 years of age in northern Sweden. *Diabetes Medicine* 2002 Oct; 19 (10):874-80.

- Epstein, Steven (1996) *Impure Science: AIDS, activism and the politics of knowledge*. University of California Press: Berkeley, Los Angeles & London.
- Featherstone & Burrows (1995) Cultures of Technological Embodiment: An Introduction. *Body and Society*. Vol. 1, No. 3-4.
- Fishman, Jennifer (2004) Manufacturing Desire: The Commodification of Female Sexual Dysfunction in *Social Studies of Science*, Vol. 34, No. 2.
- Fox, R.C. (1959/1974) *Experiment Perilous*. Philadelphia: University of Pennsylvania Press.
- Friedson (1970) *Professional dominance: the social structure of medical care*. New York: Atherton
- Fujimura, Joan H. & Clarke, Adele E. (eds.) (1992) *The Right Tools for the Job – At Work in Twentieth-Century Life Sciences*. Princeton University Press: New Jersey.
- Fujimura, Joan (1987) Constructing ‘Do-able’ Problems in Cancer Research: Articulating Alignment in *Social Studies of Science*, Vol. 17, 257-93.
- Gardell, Bertil & Gustafsson, Rolf Å et. al (1979) *Sjukvård på löpande band. Rapport från ett forskningsprojekt om sjukhusets vård- och arbetsorganisation*. Prisma: Stockholm.
- Gassman, Oliver; Reepmeyer, Gerrit and von Zedtwitz, Maximilian (2004) *Leading Pharmaceutical Innovation: Trends and Drivers for Growth in the Pharmaceutical Industry*. Springer Verlag: Berlin and Heidelberg.
- Gaudillière, Jean-Paul & Löwy, Ilana (1998) *The Invisible Industrialist: Manufactures and the Production of Scientific Knowledge*. Basingstoke: Macmillan Press Ltd.
- Gibbons et al. (1994) *The New Production of Knowledge: The Dynamics of Science and Research in Contemporary Societies*. London: Sage.
- Gieryn, Thomas F. (1999) *Cultural Boundaries of Science: Credibility on the line*. Chicago and London: University of Chicago Press.
- Goldbeck-Wood, Sandy (2001) Commentary: changes between protocol and manuscript should be declared at submission. *British Medical Journal* 2001;322:1457-1462 (16 June)
- Goodman, Jordan (1998) Pharmaceuticals, Industry and Biomedical Research. In Löwy and Gaudillière (eds.) *The Invisible Industrialist: Manufactures and the Production of Scientific Knowledge*. Basingstoke: Macmillan Press Ltd.
- Goran, Michael I. (2000) Energy Metabolism and Obesity in *Medical Clinics of North America*, Vol. 84, No. 2.
- Gusterson, Hugh (1993) Exploding Anthropology’s Canon in the World of the Bomb: Ethnographic Writing on Militarism in *Journal of Contemporary Ethnography*, Vol. 22 No. 1, April 1993. Sage Publications.
- Hacksell, Uli & Johnsson, Gillis(1997) Från idé till färdigt läkemedel: en process på 10-15 år. *Läkartidningen*, Vol. 94, No. 28-29.
- Hampson, Ian & Junor, Anne (2005) Invisible work, invisible skills: interactive customer service as articulation work, in *New Technology, Work and Employment*, Vol. 20, No. 2.

- Haraway, Donna (1991) *Situated Knowledges: The Science Question in Feminism and the Privilege of Partial Perspective in Simians, Cyborgs and Women: The Reinvention of Nature*. New York: Routledge.
- Harding, Sandra (1987) *Feminism and Methodology*. Open University Press.
- Hartsock, Nancy C. M. (1987) The Feminist Standpoint: Developing the Ground for a Specifically Feminist Historical Materialism, in Harding (ed.) *Feminism and Methodology*. Open University Press.
- Hedqvist, Maria & Eggertsen, Robert (2002) Otillfredsställande viktreduktion med orlistat in *Läkartidningen*, Vol. 99, No. 5.
- Healy, David (2004) Shaping the Intimate: Influences on the experience of everyday nerves in *Social Studies of Science*, Vol. 34, No. 2.
- Häggglöf, Mats (2002) Läkemedelsbolag kränger onödiga piller. *Dagens Nyheter*, February 21.
- Illich, Ivan (1976) *Limits to medicine*. London: Marion Boyars Publishers Ltd.
- Jacobsson, Bengt (1998) Standardisering och expertkunskap in Brunsson N. & Jacobsson, B. (eds.) *Standardisering*. Nerenius & Santérus förlag.
- Jadad, Alejandro (1998) *Randomised controlled trials*. London: BMJ Books
- Johansson, Anna (1999) *Elefant i nylonstrumpor: om kvinnlighet, kropp och hunger*. Anamma.
- Johannisson, Karin (1997) *Kroppens tunna skal: sex essäer om kropp, historia och kultur*. Norstedts förlag.
- Johnson, Ericka (2004) *Situating simulators: The integration of simulations in medical practice*. Lund: Arkiv.
- Kallings, Lena V (2002) Åtgärder mot fetma – Nationell inventering av pågående studier/projekt avseende fysisk aktivitet och kost för att förebygga övervikt och fetma. *Statens Folkhälsoinstitut 2002:6*.
- Latour, Bruno & Woolgar, Steve (1979) *Laboratory Life: The Social Construction of Scientific Facts*. Beverly Hills: Sage.
- Latour, Bruno (1987) *Science in Action: How to Follow Scientists and Engineers through Society*. Cambridge: Harvard University Press.
- Le Carré, John (2001) *The Constant Gardener*. London: Hodder & Stoughton.
- Lemne, Carola (1991/1997) *Handbok för kliniska prövare*. Studentlitteratur.
- Lewis, Jane (1993) Feminism, the Menopause and Hormone Replacement Therapy in *Feminist Review* No 43.
- Lexchin, Joel (1999) Hear No Secrets, See No Secrets, Speak No Secrets: Secrecy in the Canadian Drug Approval System in *International Journal of Health Services*, Vol. 29, No. 1.
- Leydesdorff, Loet, and Henry Etzkowitz (1996) Emergence of a Triple Helix of University-Industry-Government Relations. *Science and Public Policy* Vol. 23, No. 5.

- Lissner, L et al. (2000) Social mapping of the obesity epidemic in Sweden. *International Journal of Obesity*, No. 24.
- Lovejoy, Meg (2001) Disturbances in the Social Body: Differences in Body Image and Eating Problems among African American and White Women. *Gender & Society*, Vol. 15, No. 2.
- Lupton, Deborah (1991) *Risk*. London: Routledge.
- Löwy, Ilana (1996) *Between Bench and Bedside: Science, Healing, and Interleukin-2 in a Cancer Ward*. Cambridge and London: Harvard University Press.
- Läkartidningen* 1995-2001
- Maggio, CA & Pi-Sunyer FX (1997) The prevention and treatment of obesity: application to type 2 diabetes. *Diabetes Care*, Vol. 20, No. 11.
- Marks, Harry M. (1997) *The Progress of Experiment: Science and Therapeutic Reform in the United States, 1900-1990*. Cambridge University Press.
- Martin, Emily (1991) The Sperm and the Egg: How Science Has Created a Romance Based on Stereotypical Male-Female Roles. *Signs* Vol. 19, No. 3.
- Maynard, M. and Purvis, J. (1994) *Researching Women's Lives from a Feminist Perspective*. London: Taylor & Francis.
- Mirowski, Philip and Van Horn, Robert (2005) The Contract Research Organization and the Commercialization of Scientific Research. *Social Studies of Science*, Vol. 3, No.4.
- Mol, Anne-Marie (2002) *The body multiple: ontology in medical practice*. Durham and London: Duke University Press.
- Moynihan, Ray; Heath, Iona & Henry, David (2002) Selling sickness: the pharmaceutical industry and disease mongering. *British Medical Journal*, Vol. 324, 13 April, 2002.
- Medical Products Agency (1998) Läkemedelsverkets läkemedelsmonografi över Orlistat. *Information från Läkemedelsverket* 1998; 9(6). ISSN 1101-7104.
- Mueller, Mary-Rose (1997) Science versus care: Physicians, nurses, and the dilemma of clinical research i Elston, Mary Ann (red.) *The Sociology of Medical Science and Technology*. Oxford: Blackwell Publishers Ltd.
- Murphy, Nancy & Canales, Nancy (2001) A Critical Analysis of Compliance. *Nursing Inquiry*, Vol. 8, No. 3.
- Nählinder, Johanna (2002) Innovation in Knowledge Intensive Business Services: State of the art and conceptualisations. *Tema-T Working Paper* Nr 244.
- Oakley, Ann (1989) Who's afraid of the randomized controlled trial? Some dilemmas of the scientific method and 'good' research practice in *Women and Health*, Vol. 15, No. 4.
- Orbach, Susie (1984/1998) *Fat Is a Feminist Issue: the anti-diet guide for women*. London: Arrow.
- Oudshoorn, Nelly (1994) *Beyond the Natural Body: An Archeology of Sex Hormones*. London and New York: Routledge.
- (2003) *The Male Pill. A Biography of a Technology in the Making*. Durham and London: Duke University Press.

- Ostrander, Susan A. (1993) "Surely you're not in this to be helpful": Access, Rapport and Interviews in Three Studies of Elites. *Journal of Contemporary Ethnography*, Vol.22, No.1.
- Pfaffenberger, Brian (1992) Social Anthropology of Technology in *Annual Review of Anthropology*, Vol 21.
- Pope, Catherine (2003) Resisting evidence: the study of evidence-based medicine as a contemporary social movement in *Health: An Interdisciplinary Journal for the Social Study of Health, Illness and Medicine*, Vol. 7, No. 3.
- Rapp, Rayna (1997) Real-Time Fetus: The Role of the Sonogram in the Age of Monitored Reproduction in Downey & Dumit (eds.) *Cyborgs & Citadels*. School of American Research Press.
- Ruppel Shell, Ellen (2002) *Fat Wars: The Inside Story of the Obesity Industry*. London: Atlantic Books, 2002.
- Sachs, Lisbeth (1998) *Att leva med risk: fem kvinnor, gentester och kunskapens frukter*. Stockholm: Gedin.
- SBU report (2002) Fetma – problem och åtgärder. En systematisk litteraturöversikt. *The Swedish Council on Technology Assessment in Health Care*. SBU report 2002, No. 160.
- Schwartzman, Helen (1993) *Ethnography in Organizations*. Qualitative Research Methods Series 27. Sage Publications.
- Shapin, Steven (1989) The Invisible Technician. *American Scientist*, Volume 77, 554-563.
- Smith, Dorothy (1988) *The Everyday World as Problematic: A Feminist Sociology*. Milton Keynes: Open University Press.
- Sobal, Jeffrey (1995) The Medicalization and Demedicalization of Obesity in Maurer, ILD. And Sobal, J. (eds.) *Eating Agendas: Food and Nutrition as Social Problems*. Hawthorne, New York: Aldine de Gruyter.
- Socialstyrelsen (2000) Läkemedel i användning – förändringar och tendenser. Kvartalsrapport 2000:3.
- SOU (2000) Den nya läkemedelsförmånen. *Statens offentliga utredningar* 2000:86.
- Star, Susan Leigh (1991a) Power, Technology and the phenomenology of convention, in Law, John (ed.) *A Sociology of Monsters, Essays on Power, Technology, and Domination*. Routledge.
- (1991b) The Sociology of the Invisible: The primacy of Work in the Writings of Anselm Strauss in Maines, David R. (Ed.) *Social Organization and Social Process: Essays in Honor of Anselm Strauss*. New York: Walter de Gruyter, Inc.
- (1995) Epilogue: Work and Practice in Social Studies of Science, Medicine, and Technology in *Science, Technology and Human Values* Vol. 20, No. 4, Autumn 1995.
- Star, Susan Leigh & Griesemer, James (1989) Institutional Ecology, 'Translations' and Boundary Objects: Amateurs and Professionals in Berkeley's Museum of Vertebrate Zoology, 1907-1939. *Social Studies of Science*, Vol. 19, No. 3.

- Stearns, Peter N. (1997) *Fat History: Bodies and Beauty in the Modern West*. New York University Press: London & New York.
- Strauss, Anselm (1985) *Social organization of medical work*. The University of Chicago Press: Chicago and London.
- Thelander, Sabrina (2001) *Tillbaka till livet: Att skapa säkerhet i hjärtintensivvården* Lund: Arkiv.
- Timmermans, Stefan & Leiter, Valerie (2000) The Redemption of Thalidomide: Standardizing the Risk of Birth Defects in *Social Studies of Science* Vol. 30, No.1.
- Van der Geest, Sjaak, Whyte, Susan Reynolds & Hardon, Anita (1996) The Anthropology of Pharmaceuticals: A Biographical Approach in *Annual Review of Anthropology*, Vol. 25.
- Van Kammen, Jessika (2000) *Conceiving Contraceptives: The Involvement of Users in Anti-Fertility Vaccines Development*. University of Amsterdam.
- Varma, Roli (2000) Changing Research Cultures in US. Industry in *Science, Technology and Human Values*, Vol. 25, No. 4.
- Wajcman, Judy (1991) *Feminism Confronts Technology*. The Pennsylvania State University Press.
- (2004) *TechnoFeminism*. Polity Press.
- Webster, Juliet (1995) What Do We Know About Gender and Information Technology at Work? *The European Journal of Women's Studies*. Sage Publications (London, Thousand Oaks and New Delhi), Vol. 2, 1995: 315-334.
- Willems, Dick (1998) Inhaling Drugs and Making Worlds: A Proliferation of Lungs and Asthmas in Berg, M. and Mol, A (eds.) *Differences in Medicine: Unraveling Practices, Techniques, and Bodies*. Durham and London: Duke University Press.
- Wenger, Etienne (1998) *Communities of Practice: Learning, Meaning and Identity*. Cambridge University Press.
- WHO MONICA Project: geographic variation in mortality from cardiovascular diseases. Baseline data on selected population characteristics and cardiovascular mortality, *World Health Stat Q*. 1987;40(2):171-84.
- WHO report (1997) Obesity. Preventing and managing the global epidemic. Report of WHO Consultation on Obesity, Geneva, 3-5 June 1997, WHO/NUT/NCD/98.
- Wing, RR et al. (1985) Behavior change, weight loss, and physiological improvements in type II diabetic patients. *Journal of Consulting and Clinical Psychology*, Vol. 53, No.1.
- Åsberg, Cecilia (2005) *Genetiska föreställningar: mellan genus och gener i populär/vetenskapens visuella kulturer*. Linköping Studies in Arts and Science 303.
- Örn. Peter (1999) Skilda synsätt på forskningsetik upphov till långdragen konflikt. *Läkartidningen*, Vol. 96, No. 42.