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Ethical Regulations of Medical Research Involving Human Subjects: Exploring the Perspective of Trial Participants

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ABSTRACT

In this paper I address the question of whether the existing ethical regulations of clinical research ensure protection and well-being of human subjects. Drawing on ethnographic data gathered in Berlin, Germany, I show that German institutions which are meant to ensure the ethical validity of clinical research cannot address posed issues. It appears that these institutions (Berlin Ethik-Kommission in particular) only evaluate research protocols and do not consider the broad spectrum of processes and interactions involved in clinical research. The experience of professional human subjects, as well as the consideration of the every-day life in a clinic, shows that there is much more to clinical trials. The argument of this paper is that the inability of institutions to address protection of human subjects originates from the bureaucratic logic of their organization. Drawing on Bauman's (1992) argument that the bureaucratic machine is characterized by separation between morality and purpose, with the example of Berlin Ethik-Kommission, I argue that the bureaucratic machine cannot be sensitive to morality and ethics, even if these are its main purposes.

Keywords: commercialized clinical research, ethical regulations, biomedicine, critique of modernity, participant observation

The industry of commercialized clinical research has expanded in the last two decades. As QuintilesIMS Institute (2016) reports, the global Pharmaceutical market reached US$1.11 trillion in 2015 and is expected to reach US$1.5 trillion by 2021. With rising markets and expanding industry, there is an increasing demand for clinical trials to test new drugs worldwide. Simultaneously there is a worldwide increase in the productivity of research and development among pharma and biotech companies, due to the "growing collaboration between manufacturers and regulatory authorities to align on clinical trial design" (EvaluatePharma 2016, 27). Whereas the industry is optimistic about its success, scholars of social science have addressed issues of exploitation and unethical research in the pharmaceutical industry (see e.g. Elliott 2017, Abadie 2010, Petryna 2009, Elliott & Abadie 2008, Petryna 2006). Whereas scholars like Petryna (2006) study ethical dilemmas in the arena of global human subject research, and scholars like Elliott and Abadie (2008) focus on the situation in the United States, I seek to approach ethical dilemmas of clinical research in Germany, specifically in the federal state of Berlin. Gainotti and Petrini (2010) argue that compared to US regulations, European legislation guarantees more security to research participants, at least in respect to insurance of human subjects. It is particularly interesting to consider Germany, as one might expect it to have more advanced regulations. Given the fact that Germany is a birthplace of the Nuremberg Code - "the most important document in the history of the ethics of medical research" (Shuster 1997, 1436), one might believe that Germany would be particularly careful with the protection of human subjects.

Drawing on the data gathered during my ethnographic study, I will show that German institutions, which are meant to ensure the ethical validity of clinical research, cannot address several important issues. It appears that these institutions neglect the actual practices (in sense of Bourdieu 1977) of commercialized clinical research, since they only evaluate research protocols and do not consider the broad spectrum of processes and interactions involved in clinical research. The experience of professional human subjects shows that there is much more to clinical trials than these institutions are considering. The argument of this paper is that the inability of institutions to address the protection of human subjects originates from the bureaucratic logic of their organization. Drawing on Bauman's (1992) argument that the bureaucratic machine is characterized by separation between morality and purpose, by using the example of Berlin Ethik-Kommission (ethics committee), I argue that the bureaucratic machine cannot be sensitive to morality and ethics, even if these are its main purposes.

This paper is focused on professional healthy human subjects involved in Phase 1 clinical research. As Phase 1 trials are first in-human studies to determine drug safety, higher doses of drugs are tested on this Phase (Joffe & Parks 2009). Less than 10% of products entering Phase 1 testing reach the market (ibid). Given the high failure rate, most of the drugs that are tested in the Phase 1 are either not safe or not efficient, which means that professional human subjects are potentially exposed to high risks. Therefore, it is important to address the protection of professional healthy human subjects. This paper can be seen as a contribution to the ethical evaluation of the delicate situation of human subjects in clinical research.

The Ethical Regulation of Clinical Trials in Germany and Berlin

According to Deutsch and Lippert (2010), regulations of the conduct of clinical trials in Germany are similar to those in other member states of the European Union (ibid., 321). In this context, the Directive on Good Manufacturing Practice (GMP) (ISPE 2018) and the Guidelines

Good Clinical Practice (GCP) (ICH 1996) are considered guiding documents. However, the German law also takes the Declaration of Helsinki (World Medical Association 1964) into account (ibid., 245). "Das deutsche Arzneimittelgesetz" (the German Pharmaceutical Law) formulates that it is a function of the Ethik-Kommission to protect volunteers from excessive risk of physical injury, ensure informed consent, and secure the privacy of human subjects. This goes hand in hand with the concept of research ethics committees, introduced after the first revision of the Declaration of Helsinki, Article 23, in the year 1975. However, in the German law, the Ethik-Kommissionen (ethics committees) are not thought to monitor clinical trials as prescribed in the Declaration. The law offers no clear guidelines regarding how Ethik-Kommissionen should be built or behave. It is a responsibility of "Länder" (German federal states) to build Ethik-Kommissionen, and it is a responsibility of Ethik-Kommissionen to interpret the law.

Specifically in Berlin, as an interview with Dr. Stoeter (2017) revealed, the Ethik-Kommission is primarily concerned with procedural questions. It is there to evaluate research protocols to ensure that the risk of harm to human subjects is minimized, to define who can participate as a human subject, and to confirm the amount of "Aufwandsentschädigung" (expense allowance) for participation. The Berlin Ethik-Kommission is not capable, however, of regulating the conduct of a trial once it has started. After a trial begins, it is the responsibility of an "Überwachungsbehörde" (surveillance authority) to make sure that formalities are respected, that no violations are taking place, and that the clinical trial company provides accurate reports. However, the "Überwachungsbehörde" does not monitor each trial conducted in Berlin, but instead only samples studies randomly and investigates those that caused complaints. The Ethik-Kommission is also not responsible for monitoring and evaluating all processes that happen before and after the trial, such as recruitment strategies used by companies conducting clinical research.

Methods

To study the question of whether the existing ethical arrangements ensure the well-being of human subjects, I draw on the data gathered during my fieldwork. I approach this question through observations made in Berlin, Germany. In the context of Germany, Berlin is a poor city with the fourth highest Armutsgefährdungsquote [approx. 'risk of poverty rate'; an indicator used to measure relative income distribution in Germany] among German federal states for the year 2016. Berlin's Armutsgefährdungsquote was 19.4, while the median and mean rates for Germany overall were 16.95 and 16.9125, respectively (Statistisches Bundesamt 2017). This might be one of the factors which influences the availability of larger pools of potential human subjects. Since I am studying medical ethics in a German context, through the case of Berlin, the core of my argument is inductive in its logic. This paper is explorative in nature, because there has been very little ethnographic work dealing with the life-experience of human subjects involved in clinical trials in Germany; Sachs's (2015) journalistic dairy was the only other example I could find. Given these two factors, qualitative methods have been used. I engaged in one month of fieldwork and conducted one semi-structured interview with an expert.

Most of the empirical findings presented in this paper are the results of my fieldnotes. My aim was to study how commercialized clinical research works for its participants. As thinkers such as Max Weber and George Herbert Mead have argued, it is essential to understand how human beings make sense of social processes and use structures, systems and institutions (Gardiner 2000, 4). Inspired by Gardiner's claim that "everyday life deserves to be taken seriously and is worthy of intensive study in its own right" (ibid., 207), I decided to engage in an analysis of how commercialized clinical research works for its participants: human subjects. Apart from engaging in participant observation in the field of clinical research, I closely consider the biographies and experiences of my two key informants, Elli and Katz (pseudonyms). While presenting their portraits, I seek to promote a more intimate

manner of engaging with research informants. Particularly inspired by Kapoor's (2004) interpretation of Gayatri Spivak's writings, I prioritized face-to-face encounters and attempted to reduce the intensity of the process of objectification. In my role as participant observer, I followed the enrolment process for a clinical trial at CTCB (fictitious name):[1] completed the registration procedure, visited the "Infoveranstaltung" ['information event'; refers to the event where potential human subjects are invited to learn about the trial they have applied for], did the "Voruntersuchung",[2] and talked to people in the field. As a coding technique, I have used open coding (see Emerson et al. 2011, 171), which gave me an opportunity to engage open-mindedly with the analytic dimensions, categories and concepts and comprehend the relations between them.

Regarding the expert interview, I conducted an interview with Michael Stoeter, M.D., who works for the Ethik-Kommission in Berlin. The information obtained gives essential insight into responsibilities and tasks of Berlin Ethik-Kommision. One of the central limitations of this fieldwork and the interview is related to language since German is not my mother-tongue. The scope of this work is also limited since both my key informants come from Ukraine, and thus, are representative of a very specific population. The main challenge I had to face during my research was to establish a reflexive approach – in sense of Kapoor (2004) – when interacting with my informants. Especially with regard to how I obtained the data, I recognize my lack of skill in self-reflexivity.

Fieldwork

I now want to describe what clinical trials are like for their participants. I first briefly introduce recruitment strategies used by clinical trial companies that I encountered during my fieldwork. I then bring my own experience of enrolment at the CTCB clinic, as to give a glimpse into the everyday practices at a company conducting clinical trials. Central to my fieldwork is the consideration of experiences of professional human subjects, since it provides insight into their logic, reasoning and attitudes. I seek to build my argument essentially by bringing profiles of my key informants Elli and Katz into the spotlight.

Recruitment Strategies

My fieldwork has shown that companies that are conducting commercial clinical research use various recruitment strategies. They advertise in public places, target networks and reinforce participation of those who are already in their database. CTCB and CKP (fictitious name), for instance, advertise in Berlin train stations and in public transport. CTCB also rewards those trial participants who recruit new volunteers: he or she could receive additional compensation ranging from 50 to 200 Euro (with the top rate applying if one finds a healthy human subject older than 60), on the condition that the new-comer completes the study successfully. Trial companies also reinforce participation of those who previously expressed interest in participation. Within four months of sharing my contact information I received 7 e-mails and 4 letters regarding trials in CTCB. NVS (fictitious name) sent me 21 e-mails promoting their clinical trials and 1 e-mail encouraging me to recruit other volunteers to win a new Apple iPhone 7. Companies may use innovative advertising strategies as well such as advertising on Instagram: presumably because of my browsing activity I noticed a "sponsored post" on my news feed saying that people with a dermatological illness could receive nearly 4.000 Euro at CTCB.

Enrolment Process

In order to give proper insight into the realities of clinical trials research, I will now introduce the enrolment process I went through myself. To enrol for a study at CTCB, I filled in an online application and received a call from the recruitment team the following day. On the phone, I answered a questionnaire, which included questions regarding my personal details, medical history, nationality and skin colour. Interestingly, when I was telling the man on the phone my height and weight, he then sounded encouraged, because my BMI-Index was appropriate. He was also encouraged later on when I said "no" to all illnesses and disorders he listed. Just for the record, I did not know what most of these illnesses and disorders were, not least because of the complicated medical language. I tried to ask the meaning of some of them, but the list was so exhaustive, and the telephone situation was not conducive to lengthy conversation. My informant Katz advised me to deny any prior illness or disorder

to maximize my chances to be invited for the next stage of enrolment, saying: "They will not figure it out anyways". At the end of the telephone interview, I received an invitation for "Infoveranstaltung" for a Phase 2 study - which demonstrates the relative safety and efficiency of a new drug (Seely & Grinspoon, 2009) – for human subjects with iron deficiency which would take place in some four days.

Arriving at the "Infoveranstaltung" at the CTCB clinic, one needs to pass the reception before heading to the room of the event. People that are not invited cannot enter; they are first asked at the reception where they are going, and their ID-Cards are then checked in the room of the event to make sure that only registered people attend. The "Infoveranstaltung" was run by the doctor who was in charge of the conduct of the trial. The doctor referred to a PowerPoint presentation behind him. One of the first things we were asked when the "Infoveranstaltung" began was whether some of us participated in trials before. From 16 people in the room, at least four had experience with other trials (consider that this event was for a Phase 2 trial). Recalling my fieldnotes:

> My general impression was that the doctor didn't try to explain to us many of the details, especially not regarding the medication itself. We are supposed to know how we proceed, what should we do and what should we not do. Side-effects were named at such a fast speed that I could barely switch from one topic to another. But I should acknowledge that they gave us this thick bunch of papers explaining a lot of stuff. I'll take a look at home (from fieldnotes 02.02.17).

The thick bunch of papers had 62 pages, which included the informed consent form for participation in the trial, information regarding CTCB, involved sponsors, insurance, the rules of the clinic, and information on the medication that was being tested and its side-effects. We were also instructed on preparations for the "Voruntersuchung", which included restrictions on our physical activity as well as our eating and drinking habits.

The "Voruntersuchung", which happened couple of days later, was held in a very efficient environment. When I arrived at the receptionist's desk, a woman who was introduced to me as a doctor asked me whether I had any questions regarding the trial. There were people waiting behind me and the environment was not created for an in-depth talk regarding the trial. In a hurry, I signed the consent form and was asked to show my registration certificate ("Anmeldebescheinigung").[3] I showed a pdf document on my smartphone and no other questions were asked. I took a seat in a small waiting room, which was not completely a room, but part of a corridor. There was an awkward PTT – Pneumatic Tube Transport – through which nurses would exchanges boxes of test tubes filled with the blood of potential human subjects for empty ones. The PTT machine was making noises which I and some other people in the room doing the "Voruntersuchung" found funny. Just next to us there was the room where blood was taken. The door was mostly open, and one could see the three tables where nurses were more like supermarket-cashiers: they were taking blood from people and ringing filled test-tubes up with the same "Beeep" sound produced by a supermarket checkout. After I had my own blood taken, I waited in the room listening to "supermarket" sounds, the ridiculous PTT-machine and a radio, which was set to a channel playing the kind of music used to try and create a "positive atmosphere" (reminding me of a supermarket again). Afterwards I was told to proceed with electrocardiography, which took place in a curtain-walled room with two beds. Just as at the blood station, the environment was very efficient:

> Nurse made me undress, not particularly friendly and wasn't very gentle with electrodes. When the machine was connected to me, she didn't cover my feet, so I felt a bit cold, but was not allowed to move. And the nurse seemed busy, and left me in the room alone very soon, so I didn't have a chance to ask (from fieldnotes 16.02.2017).

After the electrocardiography was performed and I started putting my clothes on, the next

potential human subject was already in the room. This approximately 55-year old woman was asked to start undressing and she seemed more confused about the procedure than me. The nurse only mentioned that we both are girls and there is not much to be ashamed of. The final stage of the "Voruntersuchung" was the private visit to the doctor in his office, where I was asked about my health and where I could at last ask questions about the medication which would be tested.

Professional Human Subjects

Professional human subjects are those who participate in three or more usually Phase 1 clinical trials per year. They know what to do to raise their chances of being recruited as a human subject. As my key informant Katz indicated, sometimes these people participate in clinical trials for different firms in different German cities, such as Berlin, Mannheim, Ulm and others. Professional human subjects often disregard non-participation recommendations: they either do not report that they have been participating in a trial recently, or they enrol for another study before they are allowed to, or they engage in parallel trials.

Katz. A 42-year-old professional human subject, Katz engages in four trials per year and his livelihood depends on this income. Katz comes from Ukraine and is fascinated by life in Germany. He currently has a semi-legal status in Germany. Having a Polish visa (which is known to be easier to obtain for Ukrainians), he is not registered in Germany. The story of Katz's involvement in trials traces back to 2002 when he was first introduced to the industry of commercialized clinical research by his brother. Interestingly, his brother learned about trials in a German "Kneipe" (pub or bar) when he was out drinking beers with his friend: they accidentally met a woman who happened to work in CTCB. She told them about her job and about the opportunity for a free health-check ("Voruntersuchung"), which they were then invited for. Very soon Katz's brother visited CTCB and shared information about "easy money" with Katz.

In our talks, Katz recalled that at that time, coming from Ukraine, he could not believe this was a real opportunity. They (the clinical trial company) give you a place to stay, they feed you, and they also take great medical care of you – "what's the catch?". At that time Katz was still trying to establish his life in Ukraine, switching between jobs like driver and cook which he found very physically demanding and too poorly paying. For more than 7 years he worked as a driver for an oil company, driving an old truck (made in the USSR) on the poorly-equipped bumpy roads of Ukraine. Katz acknowledges that this job caused problems to his spine. His 3-year-long employment as a cook demanded he spend hours on his feet. Given this job experience in his country, Katz developed a logic that every job available to him would have a negative effect on his body. Katz does not deny the fact that his engagement in clinical trials might result in side-effects; "but so will every other job", so in the end it did not make much difference for him. In 2013 Katz decided to give up his house, two dogs and friends in Ukraine and move to Germany with his girlfriend to enjoy the country's better living standards. "It's easier to learn another language than to make a change in my country," he said. Katz sees life as too short to struggle for survival in Ukraine, so he prefers to look for opportunities abroad. After the experiences that Katz had in his country, engagement in clinical trials appeared to be an easy, and sometimes even pleasurable, source of income.

Elli. Elli is another professional human subject from Ukraine. This 30-year-old woman has a degree in law but has never worked in this field. In her country, she used to make a living by giving manicures and pedicures. Now she is in Germany with a semi-legal status. She is not registered here and thus cannot acquire a "normal" job, however she can still earn her livelihood with clinical trials without violating the law. Like Katz, Elli too sees her engagement with them as a job, as an incident which happened during her participation in one trial at CTCB demonstrates. At the trial, there was a woman who wanted to sleep with the window open, but other human subjects in the room expressed objection to this. The woman then decided to talk to the nurse to find a solution, like a different room. When she came to the nurse and asked for a separate room, "the nurse had looked at her as if she asked for something extraordinary". While the woman

was puzzled at the reaction of the nurse, Elli was puzzled too, but at the reaction of the woman: "What do these people expect? It is a job, they are paid for it!"

Elli's first trial was conducted in 2014. She usually engages in two or three trials per year and seems happy about her occupation. Through clinical research, she does not just make her living, but also has opportunities to travel around Germany, monitor her health, even gets the feeling that she is helping humanity. Elli was particularly proud of her participation in a study about the testing of a medical product for asthma patients.

As Elli and Katz's profiles show, people in economically disadvantaged conditions are ready to accept the side effects of their occupation. Moreover, these people show a high degree of compliance and obedience, and thus can be seen by companies conducting clinical research as a godsend. They will do their best to have perfect physical indicators to have a chance to participate in a trial, and will likely be the last ones to refuse to continue to participate. According to Katz, robbers and bottle collectors (for "Pfand")[4] are present during trials, which might indicate that it is often people who struggle with economic survival who participate in commercialized clinical research.

Body Treatment and Manipulation

Professional human subjects are aware of what kind of physical indicators they need to raise their chances of participation in clinical trials and know how to achieve demanded results. In general, body treatment involves committing yourself to a healthy lifestyle, like healthy food, occasional jogging and gym use. Even though smokers are allowed in some clinical trials, professional human subjects usually do not smoke at all. Katz occasionally smokes, but he has never reported it to any of the clinical trial companies he engages with. A few days before a "Voruntersuchung" or a trial, he does not touch cigarettes. Alcohol and drug consumption among professional human subjects is usually avoided in general or "paused" before and during the clinical trial.

Apart from engaging in a more or less healthy lifestyle, professional human subjects engage in direct body manipulation. The body mass index (BMI) is sometimes targeted. Elli is a tall and slim woman, and before the "Voruntersuchung" she eats a lot of Syrniki (fried quark pancakes, usually consumed together with sour cream or jam) to achieve more weight and improve her chances of being recruited. On the day of a "Voruntersuchung" she drinks a lot of water (2 litres in one morning) to be heavier for tests. Specific physical indicators are sometimes targeted for direct manipulation. With the help of the Internet, trial volunteers figure out such delicate questions as those regarding drug consumption. One of my participants, a professional human subject and a regular cannabis consumer, used the Internet to find out how to lower the THC indicators in his urine within five days. When it comes to more specialized information, one may consult professionals. Elli, for instance, was consulting doctors in her home country on how to improve certain blood indicators. It is also not uncommon to consult those who work for the company conducting clinical trials. Katz, for instance, adopted a very social, polite and respectful approach in his interaction with employees of companies conducting trials in Germany – he knew them by name, brought them chocolate and chit-chatted with them. As a result, he was getting valuable advice on what was needed to maximize the chances of being recruited.

Certain manipulations of physical indicators of human subjects are also initiated by doctors from companies conducting clinical research. Katz told me about a very interesting incident that happened to him. After participation in a "Voruntersuchung" for a trial he wanted to enrol for, he received a call from a clinical trial company. The doctor explained that Katz's physical indicators were good, but unfortunately, he had low iron indicators. The doctor said they would provide him with the necessary medication to improve his indicators for free if he wanted. Katz agreed, picked up the "iron pills", took them for a week and participated in the trial afterwards.

Sometimes the manipulation of physical indicators takes the form of exploitation. Elli told me how she did a trial with a woman on

hormone medications. The trial was about testing a contraceptive pill for women and participants were supposed to take no other hormone medication. Elli was sharing a room with a woman, who already had gone through menopause and was thus not eligible for participation. By taking her own medications, the woman achieved appropriate physical indicators and was allowed to participate. She never reported this manipulative act to the doctors as they would have "kicked her out" of the study. It is not clear, though, if the woman systematically engages in manipulations of her physical indicators to participate in clinical trials and I cannot contextualize her behaviour, since I have not encountered her myself.

One of my respondents shared a story about how he falsified test results. His income was mainly generated from clinical trials and for long time he was actively involved in being a professional human subject. At some point in his "career" when he was applying for the next clinical trial, one of the tests revealed that he had pancreas issues. As a result, he got rejected for the study he applied for; moreover, he landed on a black list as an unhealthy human subject and was therefore not able to participate in the studies at this company. To take himself off the black-list he was taking medications to normalize the figures. He also forged a certificate from a doctor to prove that he had no problems with pancreas. After sending the document to the company conducting clinical trials, he was removed from the black list and could participate in trials again. It is worth mentioning that the pancreas incident occurred at the time when he was engaging in parallel trials, however, this informant was "not sure" whether his problems were the outcome of participating in more trials than recommended, whether it was a particular trial, or whether it might have been the unrelated result of his own health. The informant never reported these possible side-effects to the companies that tested medication on him at that time, because he was aware that he violated the non-participation agreement and considered the outcome to be his own fault. This participant still takes medication to normalize indicators for his pancreas and continues to participate in trials.

During my fieldwork I heard about another example of falsification of information related to physical indicators. This time the falsification was initiated by the doctor. A man of 57, a German citizen whom I met in the waiting room of CTCB, had just completed a trial and was telling me about an incident that happened to him. At the beginning of one trial he had low blood pressure and was therefore not eligible for participation in the study. Usually there are "Ersatzprobanden" (replacement volunteers) for every trial, but there was none for the given trial due to the lack of appropriate volunteers. When the nurse discovered that the man had low blood pressure she consulted the doctor on whether she should include it in the protocol. The doctor replied that it was needless to mention this information and that the volunteer should be able to participate in the trial. This example shows how sometimes, due to the lack of volunteers, certain points of research protocol regarding the demanded indicators can be neglected.

Discrepancies Between the Perspectives of Institutions and Human Subjects

The main task of the Ethik-Kommission in Berlin is to evaluate the research protocol to make sure that risk of harm is minimized. My criticism (and not only mine: see Elliott & Abadie 2008, Petryna 2006 etc.) is that ethic commissions, or review boards (in case of other countries), are only concerned with the research protocol. My fieldwork has shown that the interaction between the companies conducting clinical trials and potential/actual human subjects begins before, and does not stop after, the actual conduct of the trial. Relations that arise during the recruitment, enrolment, "Voruntersuchung" and after the trial are eliminated from the responsibilities of Ethik-Kommission and are therefore not subject to ethical evaluation. The company conducting clinical trials can use various strategies for recruitment that go unreviewed for their ethical validity. In fact, these strategies are used to promote professionalization of the role of being a human subject and encourage trial

participants to recruit people from their own personal networks. Advertisements in public places certainly target specific demographics through the way they are located. Paying human subjects for providing a new volunteer might motivate trail participants to provide extra instructions to new participants on how to enrol and perform competently, which will raise the chances that he or she will enter the field knowing how to behave and complete the study. Finally, numerous e-mails and letters encourage professionalization among human subjects. People from databases are regularly reminded of clinical trials and they are exposed to honoraria they could receive for participation. One last point: it could also be the case that certain advertisements might have promoted illness among potential human subjects. A CTCB Instagram advertisement for a dermatological illness trial that promised nearly 4000 Euro for participation could possibly encourage certain populations to acquire the ailment just to allow for participation. The telephone interview and the "Infoveranstaltung" are also not examined by the Ethik-Kommission. During my fieldwork at various stages of my own enrolment process I encountered situations that I found disturbing and somehow wrong. First, the encouragement on the phone from the recruitment team might impact the answers of potential human subject. Second, the "Infoveranstaltung" was not meant to give me an understanding of what kind of medication was being tested, but rather of the conduct of experiment and house rules of the clinic. Finally, at the "Voruntersuchung" I experienced everyday life at a company conducting clinical research. In this highly depersonalized, efficiency-oriented environment, human subjects are not seen as individuals whose private sphere and emotional well-being are of concern. Human subjects in this context appear neither as actual volunteers, nor as actual workers.

My fieldwork has also shown that the research protocol is not always fully respected. Examples such as that of the man who, despite his low blood pressure, was still allowed to participate in a clinical trial demonstrate this. Since defining who is eligible for participation is the task of the Ethik-Kommission, it is very problematic that the clinical trial company, particularly the doctor, decided to take the authority. Essentially this example shows that there is no monitoring of the conduct of clinical trials and doctors feel free to implement their own (even if minor) modifications to the research protocol. The fact that Katz was given extra medication ("iron pills") to be eligible for participation also indicates how companies conducting commercialized clinical research may use different techniques to approve more volunteers for trials. Healthy human subjects are per definition not supposed to take extra medication, and I doubt that the research protocol mentioned that it is legitimate and/or ethically justifiable to offer free extra medication to potential human subjects to improve their physical indicators.

The Ethik-Kommission may influence the definition of the healthy human subject, tolerating or not tolerating certain deviations from the perfect indicators (Dr. Stoeter 2017). My fieldwork has shown that healthy human subjects are not necessarily healthy, and their physical indicators are sometimes the targets of manipulation. Particularly in cases where the income of trial participants depends on results of the tests, appropriation of physical indicators may result in severe exploitation of health. The examples above show how indicators, such as blood consistency, can be target to manipulation. Whereas I cannot make a statement regarding how widespread these practices are among human subjects, my brief fieldwork also revealed that companies conducting clinical trials have their role to play in "creating" the perfect body, through practices such as offering free medication and "turning a blind eye" to minor deviations from demanded physical indicators. Further investigation is needed on this matter.

Dr. Stoeter mentioned that for the Ethik-Kommission it is important to make sure that there are no further benefits involved in participation in trials. My fieldwork revealed central importance of the "Voruntersuchung", which attracts certain populations and can therefore be considered a further benefit and part of recruitment strategy. People I talked to, especially those from Ukraine and Russia, were interested in doing the "Voruntersuchung" to check their health. Coming from a country with

decaying healthcare system, one is attracted the idea of a free check in Germany. The "Voruntersuchung" is also an essential element of the recruitment strategy which might "trap" the attracted populations. The way I experienced the setting is that once you enter, you "wallow", gradually developing trust to the setting and the professionals. After the "Voruntersuchung" I myself had the idea of taking part in the trial: I was familiar with the company, they seemed knowledgeable about what they do, the place was clean, and the staff seemed professional. These considerations of specific institutional settings can be linked to writings of Foucault. Indeed, medical power has capacity to appear as positive and benign, whereas its oppressiveness is obscured (Jones & Porter 1994). Even though a clinic where trials are conducted is something different from a clinic where patients are treated, both have medical power in common. During the "Infoveranstaltung" and especially "Voruntersuchung", potential human subjects encounter this specific institutional setting. Researchers at CTCB are defined as doctors; the equipment they use is that of the hospital. The professional atmosphere of the setting is meant to communicate trust, which also contributes to the elimination of fear of risk. Human subjects might not be aware that the doctor who is in charge of the trial might be no doctor at all. According to regulations, the researcher only needs to be "appropriately qualified" and have at least two years of experience in research (see Deutsch & Lippert 2010, 426). Linking it to the criticism above, one sees how the Ethik-Kommission is primarily concerned with procedural questions and with research protocol results within a narrow focus. Because of this, the significance of the "Infoveranstaltung" and the "Voruntersuchung" is neglected and these are not subjected to ethical evaluation.

Finally, in the interview, Dr. Stoeter from the Ethik-Kommission claimed that these are "tricks" of human subjects which enable the existence of professional human subjects, whom he referred to as "Proband-Touristen." The term "Proband-Tourist" – approx. "experimentee-tourist"– was particularly well-known in 80s and 90s in Germany when the problem of professionalization of trial participants was more visible. It appears that it is necessary to reconsider his assumptions on this issue. When I was talking to professional human subjects, they denied the fact that they fake their ID-Cards, register with different names or something of that sort. Elli and Katz claimed that it is relatively easy to engage in multiple trials within a short period of time and companies conducting research rarely check with the database in Freiburg. Elli also told me that clinical trial companies need to pay for this check. I tried to contact the VIP-Check[5] and ask about the conditions but received no reply. Both Elli and Katz, being on a semi-legal status in Germany, claimed that the regulations for enrolment in this regard are very easy: they were never checked for visa, and most of the trial companies in Germany do not request registration papers.

The issue with "Proband-Touristen" relates to the fact that only companies conducting clinical research see the human subject in person. As Dr. Stoeter explained, neither Ethik-Kommission, nor "Überwachungsbehörde" can see trial participants due to concerns related to privacy. "Überwachungsbehörde" can only access anonymized, pseudonymized information about human subjects, whereas the Ethik-Kommission is not thought to access this sort of information at all. However, the creation of the VIP-Check eliminates the necessity to consider "Proband-Tourismus". Dr. Stoeter claimed that this problem was acute in the 1980s and 1990s, but the establishment of a database of human subjects in Freiburg solved it. In fact, it did not, but it ended the discussion. Even if the database in Freiburg somehow improved and ensured monitoring of human subjects' participation in trials this would not solve the problem, as this may drive human subjects to other countries in Europe and conduct trials there. The creation of an EU-wide database is not expected within the next decade. This not just because such projects take years of negotiations, but also due to Brexit (Brennan 2017): the European Medicines Agency, currently located in London, will be busy with its own relocation, restructuring and recruitment of new personnel. Therefore "Proband-Tourismus" was, is and will remain an issue in Europe.

The Problem

In summary, my fieldwork revealed that the assumptions of institutions which are meant to ensure the ethical validity and well-being of human subjects in commercialized clinical research, are detached from the actual practices. Institutions and regulations are unable to address issues of exploitation. As Elliott (2017) put it, it is an ethical issue whether the human subject's poverty and desperation are taken advantage of. "To exploit someone is to take unfair advantage of them, usually in a relationship of unequal power" (ibid., 526).

When thinking of Berlin Ethik-Kommission, or any other institution meant to ensure ethical validity of clinical research, one needs to consider their bureaucratic organization. These institutions are closely linked and sometimes determined by the needs of a rapidly expanding pharmaceutical industry (see QuintilesIMS Institute 2016). As the most technically advanced type of organization, developed bureaucracy enables maximum productivity and efficacy, which is particularly desirable in a capitalist market economy (Weber 1978, 974). In this respect, bureaucratization reinforces the expansion of the capitalist market economy and vice versa. Though being productive and efficient, bureaucratic type of organization cannot be seen as a good in its own right. Bauman (1992) warns about the destructive potential enabled by the development of bureaucratic action and mentality. According to him, the most dangerous aspect of bureaucracy is the separation between morality and purpose. On the one hand, bureaucracy implies the division of labour. As a result, practical and intellectual distance between the actor and the action is created. In such a context, the action does not possess prior purpose, neither can it be subjected to moral evaluation. Moral responsibility is thus replaced with formal and technical responsibility (technisch-formale Verantwortung), which cannot comprehend the action as a mean to an end, rather action becomes an end in itself (see ibid., 113). On the other hand, bureaucracy implies dehumanization (Entmenschlichung), as it reduces the objects of its action to purely quantitative units. Human beings are reduced to numbers, which eliminates the possibility of applying rules of morality or ethics to them. Only human beings – and never numbers – can be subject to moral evaluation (see ibid., 117). Being bureaucratically organized, institutions that are meant to ensure the ethical validity of clinical research too are unable to make it ethically unambiguous. The problem arises not because Dr. Stoeter is doing a "bad job", but because ethics cannot be ensured within a bureaucratic machine due to its dynamics and logic.

The division of labour between different institutions involved in ensuring the ethical validity of clinical research, specifically between the Ethik-Kommission and "Überwachungsbehörde", does not allow either of these institutions to see the bigger picture and spot potential of exploitation. Dehumanization, in particular, highly anonymized handling of human subjects, eliminates the possibility of spotting actual individuals behind numbers and pseudonyms. For the Ethik-Kommission dealing with ethics becomes a procedural question of approving a research protocol and is thus related to formal and technical responsibility, as Bauman would put it. This ethnographic study has shown that practices of clinical research cannot be reduced to research protocol. Stories I have picked up in the waiting room at CTCB, and those my key informants shared with me, show how multi-layered the practices of clinical trials are. The distance between Berlin Ethik-Kommission and the CTCB clinic allows many minor and major violations of research protocol to happen. Ethik -Kommission is thus unable to see the actual implications of clinical research, address issues of exploitation or understand the logic of "Proband-Touristen". The bureaucratic context of the Berlin Ethik-Kommission transforms ethical approval into a mere formality.

Conclusion

But is it possible to ensure the ethical validity of clinical research? Since the bureaucratic machine is characterized by the separation of morality and purpose, it can hardly offer a solution. An option could be to target the core of clinical research itself: biomedicine, questioning its origins, biases and possibly false assumptions. Indeed, biomedicine, also

defined as modern Western medicine, is rooted in Western scientific thought (Curtis 2004: p. 36) and is therefore based on dualist assumptions and a natural-sciences methodology. Its core idea is built on Cartesian dualism (Hall 2000), which says that the body consists of a series of parts which are eventually separated from the mind and which are to be treated by doctors and biologists. Regarding methodology, modern medicine seeks to apply methods of natural science (Wiesing & Marckmann 2004). In particular it accepts the experimental approach. Central here is the idea that human biology can be used as a standard for comparison. As Margaret Lock and Vinh-Kim Nguyen (2010) rightly point out, there can be biological differences between people who make themselves available for experimentation, and those who have no need to subject themselves to clinical trials. This makes the biological comparison problematic. One might wonder how social embeddedness creates the difference between those instrumentalized for trials and those indirectly benefiting from them. It is also a question whether or how existing social hierarchies contribute to the availability of research subjects for experimentation. Further research is needed to understand how to deal with unethical clinical research.

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Endnotes

[1]CTCB is a fictious name for one of the multinational life sciences consulting firm which operates in Berlin. This company conducts clinical trials on behalf of its pharmaceutical clients to expedite the drug approval process. Here and further I hide the real name of clinics to make sure that no inconvenience is caused to my informants.

[2]"Voruntersuchung" – in English: "preliminary examination" (translated by the author) – refers to tests done to potential human subjects before clinical trial to find appropriate human subjects with demanded physical indicators. These tests usually include examination of blood and urine for clinical chemistry, haematology, hormones, infectious diseases and illegal substances. These tests are supplemented with impedance cardiography and personal talk with the doctor.

[3]"Anmeldebescheinigung" – in English: "registration certificate" (translated by the author) – is a document which proves that a foreign national is currently residing in Germany; it particularly refers to those foreign nationals who are citizens of the European Economic Area.

[4]"Pfand" – in English: "bottle deposit" (translated by the author) – is a price on a bottle that you get back if you return the bottle to a certified outlet in Germany. The amount of money varies from 0,08 to 0,25 cents.

[5]VIP-Check is a database in Freiburg created in 1990 to monitor the compliance of human subjects in Germany. According to Dr. Stoeter it is accessible to most of the clinical trial companies that conduct Phase 1 trials. See the Web-Site: http://feki.com/.

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