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University of Cape Town



Department of Social Anthropology

Protocol and Beyond: Experiment and Care during a TB Vaccine Clinical Trial in South Africa

Justin Dixon

DXNJUS001

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COMPULSORY DECLARATION

This work has not been previously submitted in whole, or in part, for the award of any degree. It is my own work. Each significant contribution to, and quotation in, this dissertation from the work, or works, of other people has been attributed, and has been cited and referenced.

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Abstract

There has been a substantial increase in the amount of biomedical research being conducted in resource-poor regions of the world since the 1980s, particularly clinical trials involving human subjects. With a particular focus on public-sector clinical trials, a number of anthropologists have recently conducted important ethnographic research into the ground-level operations of clinical research organisations and the relationships between doctors, co-ordinators, participants and non-participants. It has been argued that formal ethics and the scientific practices they govern obscure a relational and affective dimension of clinical trials, which is both necessary for, and transcends, the requirements of trial protocols. On the basis of ethnographic research with a clinical research organisation in South Africa specialising in trialling tuberculosis (TB) vaccines, I contend the explanatory value of tracing the diseases 'under the microscope' from global public health agendas to ground-level research practices when exploring the relationships between the 'ordered separations' of medical research structures and the relational-affective dimension they obscure. Through a close examination of TB at different levels of scale, I aim to open up more avenues of enquiry into the multifarious factors that shape the important relations that develop between clinical research organisations and those on whom research is conducted.

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Chapter 1:

Introduction

I. Overview

Since the 1980s, there has been a substantial increase in the amount of Western industry and government sponsored medical research being conducted in resource-poor regions of the world, particularly clinical trials involving human subjects. With a particular focus on public-sector medical research initiatives, a number of anthropologists have importantly engaged in the detailed empirical study of the local networks of sociality generated by clinical research organisations on the ground (e.g. Fairhead, Leach & Small 2006; Geissler et al 2008; Geissler & Molyneux eds. 2011). A common finding is that the “ordered separations” (Geissler et al 2008:702) that characterise both formal medical ethics and bio-scientific methodologies obscure the relations and transactions that inhere ground-level research practice, particularly the role that research organisations play in the provision of healthcare for participants. In this dissertation, on the basis of ethnographic research with a clinical research organisation in South Africa specialising in trialling tuberculosis (TB) vaccines, I contend the explanatory value of tracing the diseases ‘under the microscope’ from global public health agendas to ground-level trial protocols when considering the interface between the ‘ordered separations’ of medical research and the implicit relational dimension they obscure. Through a close examination of TB at different levels of scale, I aim to open more avenues of enquiry into the multifarious factors that make and shape scientifically relevant and ethically poignant relations in the context of globalised clinical trials.

II. Separations, Relations and Healthcare in Clinical Trials

An expanding body of anthropological literature has recently drawn attention to the uneasy union of the global neo-liberal economy, international pharmaceutical companies and regulatory bodies, charity and aid organisations, academic medical centres, independent research organisations, and low-income populations. One avenue of anthropological enquiry has drawn attention to the fact that clinical trials are no longer just a mode of bio-scientific research but a highly profitable *industry*, at the heart of which lies the ‘need’ for health data procured from human subjects to market pharmaceuticals (e.g. Cooper 2008; Fisher 2009; Petryna 2007, 2009; Petryna & Kleinman 2006; Rajan 2006). In the midst of this competitive marketplace, since the early 1990s more and more clinical trials are conducted in low- and middle-income countries, where clinical research can be conducted more cheaply than in high-income countries and where populations are, in the absence of

adequate healthcare, more likely to enrol in clinical trials and subject themselves to experimental bio-products. On the one hand, clinical trials are tightly regulated, and must adhere to stringent ethical principles and guidelines, so that vulnerable populations are protected against the pursuit of profit. On the other, Petryna (2005:184) astutely notes that ‘Big Pharma’ is now so powerful that these ethics structures are themselves malleable to global pharmaceutical interests and imperatives. Therefore, as a number of commentators have similarly pointed out, existing regulatory mechanisms are insufficient to offset the structural inequalities between ‘Big Pharma’ and vulnerable people and populations (Cooper 2008; Fisher 2009; Petryna 2007, 2009; Petryna & Kleinman 2006; Rajan 2006).

These are highly important concerns, and they are yet to be given the attention they deserve in biomedical forums with a focus on the global reach of clinical trials. Another line of anthropological enquiry approaches the overseas clinical research from a different (though complementary) angle (e.g. Fairhead, Leach & Small 2006; Geissler et al 2008; Geissler & Molyneux eds. 2011). Where the above studies (e.g. Petryna 2007, 2009) have focused on the proliferate private sector of clinical research, these anthropologists have focused their attention primarily on *public* sector medical research initiatives, which, in the context of increasingly mobile medical research structures (see below), are also becoming increasingly prevalent in the developing world. Sponsored primarily by Western governments and charities, research agendas in the public sector are usually directed at diseases of poverty (e.g. malaria, HIV and AIDS, and tuberculosis). In addition, where the former studies have attempted to draw out the trans-locality of clinical trials and the global assemblages that have ensued, the latter anthropologists, following the “ethnographic British-European tradition of social anthropology” (Geissler 2011:7), have focused on the empirical study of the ground-level operations of clinical research organisations in resource-poor regions, where global scientific and public health agendas meet local socio-economic and cultural realities.

An important finding is that the “ordered *separations*” (Geissler et al 2008:702 my emphasis) in virtue of which medical research structures are able to travel and to be implanted into a multiplicity of localities – most notably, international medical ethics codes and prevailing modes of bio-scientific knowledge production – obscure the concrete *relations* that inhere the ground-level practice of clinical research. Simpson and Sariola (2012:564-5; see also Kelly 2011:232-5) note that randomised control trials (RCTs) generate their epistemic authority through randomly allocating participants to either experimental or control groups, ‘blinding’ both medical scientists and participants to which participants receive experimental treatments, and through the rigorous adherence of preapproved trial protocols. These ordered separations generate a “‘mechanical or ‘regulatory’ objectivity” (Simpson & Sariola 2012:565) that enables the “immutable mobility” (Latour 1987) of clinical trials and, therefore, a global network of standardised clinical data. The formal medical ethics codes that are written into trial protocols in order to secure the ‘ethical soundness’ of clinical trials in resource-poor settings – such as the International Conference on Harmonization Good Clinical Practice (ICH GCP) – are similarly mobile to the scientific practices they govern. The impetus of these codes lies in

mitigating power differentials between research organisations and resource-poor populations through fostering transparency in communications about the nature of research, paradigmatically through ‘informed consent’ procedures designed to ensure that participants enrol in trials for the ‘greater good’ afforded by their participation and not, for instance, because of the material gains they might enjoy from the process (Leach & Fairhead 2011:95). Comprised of boxes to check and forms to complete, the requirements of formal ethics are “detached from its members’ social practices, and set out as principles and rules a priori; they regard separate entities (persons and groups) rather than relations and processes, as elementary particles of moral reasoning, which they frame as individual rights and decisions” (Geissler et al 2008:700). In short, the ‘ideal’ clinical trial is one which has clear-cut epistemic purposes, involving trained research personnel and willing informed participants, and taking place between predetermined enrolments and endpoints.

Contra this imagining, however, clinical research organisations, particularly those with long-standing existences in the communities in which they work, often become immersed in the dynamics of local life and the material adversities their constituents face on a day-to-day basis (e.g. Geissler et al 2008; Leach & Fairhead 2011; Kelly 2011). Geissler (2011:7) calls these networks of sociality “trial communities”, a term which deliberately unsettles the discrete entities recognised by formal medical ethics, and emphasises the emergent relations between doctors, co-ordinators, fieldworkers, participants and non-participants that unfold at the “interface” of global research structures and particular research localities. These interactions are characterised by a *relational* and *affective* dimension that demands the acknowledgement – rather than the mitigation – of the power differentials between researchers and participants. Perhaps the most important manifestation of this is that, in contexts of poor access to and delivery of healthcare, clinical research organisations often become engaged in the provision of healthcare for participants, their families and communities (Geissler et al 2008; Gikonyo et al 2008; Kelly 2011; Leach & Fairhead 2011). Kelly (2011:241), for instance, observes of the Medical Research Council’s (MRC) work in The Gambia that such is the inadequacy of primary healthcare facilities in the country that the MRC is perceived not as a research institution but as a healthcare system. True to formal medical ethics, which are distanced from and sceptical of material relations between researchers and participants, the healthcare benefits afforded by participation are largely “extra-scientific”, receiving scant formal acknowledgement and little in the way of funding (Geissler et al 2008:700). As a result, field researchers, often employed locally, play a vital, ethically charged and creative role balancing the formal requirements of protocol, the informal healthcare afforded by participation, and the fears and uncertainties of participants regarding the costs and benefits of these transactions (Fairhead, Leach & Small 2006; Molyneux & Geissler 2008:688). Obscured by both formal ethics and scientific methodologies, the trial communities upon which scientific knowledge practices are dependent are held together by substantive relations and material transactions between research organisations and the communities in which they work. These anthropologists suggest that the relational dimension of medical research be afforded a greater degree

of acknowledgement in formal ethics and the scientific knowledge-practices they govern as clinical research continues to travel into resource-poor environments.

III. Tuberculosis in South Africa

I entered this trajectory of anthropological enquiry, not out of an interest in clinical trials per se, but rather in virtue of the concern that the South African university of which I am a student has with the lived experience of TB. Tuberculosis (TB) is re-emerging as one of the most prevalent infectious diseases in the world. In 2010 alone, there were upward of 8.8 million reported cases of TB, 1.1 million deaths from TB among HIV-negative individuals, and 350,000 additional deaths among HIV-positive individuals (World Health Organisation [WHO] 2011). 95% of positive TB diagnoses and 98% of TB-related deaths happen in developing countries, where the conditions under which the disease thrives – inadequate food security, unhygienic and crowded living conditions, and poor access to healthcare – are abundant (Benatar & Upshur 2010). Although a democratic republic since 1994, a middle-income country, and with a large number of people in high-income brackets, South Africa is as yet haunted by a legacy of apartheid governance that left millions in near-absolute poverty. In conjunction with an already critical HIV and AIDS epidemic, which compounds the effects of TB, South Africa currently has the highest burden of TB in Africa, which accounts for 26% of the global TB burden (WHO 2011). In addition, while over half of reported TB cases are in Asia, certain provinces in the South Africa have amongst the highest TB morbidity and mortality rates in the world (Naidoo & Mwaba 2010:1324).

A large number of government and non-government organisations in South Africa are committed to combating the epidemic and to alleviating some of the dreadful fallout it has had on the population (e.g. South African Department of Health [SADoH], WHO, Joint United Nations Programme on HIV/AIDS [UNAIDS], *Medecins Sans Frontieres* [MSF]). Despite these efforts, the TB epidemic has nearly doubled since 2001, and in recent years, while WHO (2011) report a gradual decline worldwide in the number of morbidities and mortalities related to TB, South Africa's burden has remained comparatively stable. In conjunction with the continuing proliferation of drug resistant strains, there is a possibility that the epidemic could spiral even further out of control. The sheer magnitude of the situation is made all the more daunting by a widespread failure of treatment protocols (e.g. Directly Observed Treatment, Short-Course [DOTS]¹) in South Africa (and sub-Saharan Africa more broadly), as well as an overarching dissonance between theory and reality in public health initiatives.

¹ DOTS is an integral component of WHO's Global Stop TB Strategy, involving the direct observation of patients as they take their TB treatment by a medical professional, for at least the first two months of the drug regimen, if not the entirety. While DOTS has had some success in high-burden regions (WHO 2012), due to a lack of public health infrastructure, poverty, and poor implementation DOTS has failed to prevent the spread of the disease in certain regions such as sub-Saharan Africa (Whalen 2006).

Sitting on a board meeting in 2010 of one of the NGOs involved in combating the disease, in particular, in relation to the de-centralised TB programme in the township of Khayelitsha, Leslie London (former Director of a South African university's School of Public Health and Family Medicine) commented that little was known about what people in high-prevalence areas were actually *doing*. How did the disease punctuate their lives? What was the nature of the relations between TB-infected individuals, their families, and those who provide treatment? How did these relations play out in health-seeking environments? In short, while there has been arguably no shortage of scientific research on biomarkers of TB in recent years (e.g. research on diagnostic tools and technologies), little was known about what one might call *social* markers of TB (Macdonald 2012). What was urgently needed in order to develop a more comprehensive and sensitive response to the epidemic was a commitment to qualitative knowledge production directed at social markers of TB and their various incarnations in South Africa. In order to address this lacuna, Leslie London approached an anthropologist at a South African university, which led to a group of postgraduate students undertaking ethnographic research on social markers of TB. One of these students, I was particularly interested in exploring the intersections of social- and bio-markers of TB. Therefore, after some initial deliberations, I was put in contact with a with a clinical research organisation which I shall refer to as "The Tuberculosis Research Organisation (TRO)"².

IV. Protocol and Beyond at TRO

TRO is a clinical research organisation in South Africa established in 2001, which specialises in the trialling of TB vaccines, particularly involving infants and young children, who constitute the biggest target age-group for TB vaccines. The organisation is run primarily through its base in a large city, where they not only have extensive human resources, information technology and data management infrastructure, but also a state-of-the-art immunology laboratory from which a number of world-renowned immunological studies have been conducted. However, TRO's trials are themselves run not in the city but through its field project office, located about an hour's drive from the city in the Hareford region. TRO's field project office is situated on the premises of a public hospital in one of the most built-up towns in the area, one which specialises in TB diagnosis and treatment. The field office incorporates a vaccine trials clinic, a 15-bed case verification (CV) ward for suspected cases of childhood TB (where each 'bed' denotes both a cot for an infant and a bed for a mother or relative), an on-site immunology laboratory, and various administrative offices. TRO also has upward of thirty vehicles for, amongst other things, visiting participants in the region, bringing them to the CV ward, and transporting organic matter to and from their laboratory in the nearby city. This particular research site was chosen because of its proximity to the population from which TRO's research

² In this dissertation, all participants, institutions, healthcare facilities, and the region of South Africa in which this research took place, have been assigned pseudonyms, primarily because of the delicate relationship that TRO has with local institutions (see section VI).

participants are drawn – a several-hundred-thousand strong population with one of the highest numbers of reported TB cases in the world at present – as well as the relatively well-functioning primary healthcare facilities in the region. It is at the field project office and in the surrounding region that I conducted the bulk of my ethnographic research, which was comprised of three weeks in June of 2011 and a subsequent three weeks in June of 2012.

Upon commencing my ethnographic research with TRO, it was not long before I began to appreciate the importance that the anthropologists discussed above (section II) attribute to the substantive relations that inhere the ground-level running of clinical trials, and the transactions and challenges that easily escape the purview of social and ethical analysis. TRO's ground-level operations are inseparably tied to a legacy of apartheid governance which has left the majority of its participants in near-absolute poverty. TRO's researchers are faced with this reality day-in and day-out as their clinical research takes them into the lives and livelihoods of their participants, their families and their communities. Such are the frequencies and intimacies of the interactions between TRO's researchers and the constituents of the Hareford that, similar to the findings of other ethnographic studies (Geissler et al 2008; Gikonyo et al 2008; Leach & Fairhead 2011), the line between experimentation (distanced, objective, representational) and healthcare provision (affective, relational, transactional) has become remarkably thin. In addition, they face a number of ground-level challenges invisible from the a priori perspective of formal medical ethics. However, what I would like to argue in this dissertation – which is not readily suggested by the current literature on trial communities, but which was fostered by my entry into the study of clinical trials through the lens of TB – is that the 'interface' between global TB research and the social dynamics of the Hareford region is given shape by the particularities of TB as it transcends multiple levels of scale: global health discourse; the development of trial protocols; and as inseparably tied to a legacy of apartheid governance in the Hareford region and South Africa more broadly.

In the following chapter, I outline the global imperatives which have resulted in TRO conducting TB-related clinical trials, why the production of vaccines is of importance, and a brief history of TRO in the Hareford region – and the 'trial community' its operations have generated. I then detail the particularly complex nature of diagnosing TB in children, how these have been grappled with, and how they have been implanted into the research protocol of TRO's largest current study. In Chapters 3 and 4, the most ethnographically rich chapters, I systematically 'follow' research protocol – more so than previous studies – as it takes TRO's researchers into the most direct contact with their study participants and their communities: out with the 'follow-up teams' (Chapter 3), and in the 'CV ward' (Chapter 4). I pay particular attention to the ways in which the 'ordered separations' of protocol are intertwined with a relational-affective dimension, in which the wellbeing of participants in addition to the production of 'objective' knowledge occupies the foreground. This dimension, while often consistent with protocol (albeit implicitly so), cannot be contained within the rigid boundaries of

protocol, skirting between protocol and what I call ‘extra-protocol’³. As I will show, some of the more pressing challenges TRO’s researchers face as they conduct clinical research in the midst of often great suffering pertains to how to balance separations and relations, protocol and ‘extra-protocol’. But these challenges, and the balancing acts from which they result, are inseparably tied to the multiple levels at which TB is engaged and experienced in both its biological and socio-historical capacities. I therefore argue that studies of ‘trial communities’ in resource-poor localities be more responsive to such factors as the diseases ‘under the microscope’, which, traversing multiple levels of scale, play a significant role in shaping the scientifically relevant and ethically poignant relations that inhere the ground-level running of globalised clinical trials.

V. Research Methods

The following chapters are the product of six weeks of ethnographic research conducted primarily within the premises of TRO, the TB hospital within which it is based, as well as the surrounding rural region from which TRO’s research participants are drawn. As I mentioned above, three of these weeks fell in June of 2011, while the remainder took place in June 2012. Both of these periods of research actually fell in the middle of TRO’s current major clinical trial (the particularities of which I shall detail in Chapter 2). Thus, while I enjoyed a high degree of access to the day-to-day running of the current trial, what follows represents a somewhat embedded perspective on things during which the ‘bigger picture’ of the trial process might slip out of focus (particularly in Chapters 3 and 4). On the one hand, it would have been beneficial to have witnessed a trial from the first draft of trial protocol to final analysis and publication of the findings (which can take upward of five years). On the other, given that the notion of ‘trial community’ deliberately obscures the strict temporality of the ‘ideal’ clinical trial, I do not believe that it was necessary that I keep the entirety of the trial in the purview in order to acquire useful and relevant findings.

My approach to the day-to-day running of TRO’s current clinical trial and the methods I adopted to this end reflects some influence from actor-network theory (ANT). This influence does not manifest so much as an explicit application of the ‘theory’ – which Latour (2003:62) claims misses the point in any case – than as a set of mostly implicit pre-theoretical assumptions guiding my methodology. For instance, my entire thesis would probably be a futile endeavour if I assumed that the scientific facts are best characterised as a one-to-one correspondence between language and the world ‘out there’. Rather, I take as axiomatic that the production of knowledge for the purpose of a clinical trial is a fundamentally social and thus messy affair. Perhaps the most overtly ANT-influenced aspect of the following is my treatment of the ways in which ‘TB’ is ‘defined’ and enacted in practice (Lien & Law 2011:68), and the effects that TRO’s conceptualisations of the disease have on the day-to-day conduct

³ I use the term ‘extra-protocol’ partially as a response to Geissler et al’s (2008:700) term “extra-scientific”, in order to emphasise the day-to-day ‘beaten track’ from which the relational dimension of TRO’s operations often strays.

of a clinical trial. In order to acquire as much data as possible from my interactions in and around TRO's field office, I utilised the following research methods:

Participant Observation: Participant observation was my primary methodological tool, especially given the empirical emphasis of my research. However, because TRO's office was not open to the 'public', I committed to increasing intrusiveness of my presence as slowly and gradually as possible. I was prepared upon entering the space to spend at least the first few days simply chatting to people, performing any necessary tasks no matter how menial, and perhaps shadowing people as they went about their business. As it transpired, on my very first day with TRO one of the field teams invited me to join them as they went about conducting the 'follow-up visits', where, although I could not do much in the way of participating, bar carry a pair of scales around for the day, I was certainly encouraged to observe and ask questions about the interactions with research participants. That more or less set a precedent for the rest my research. Not only did I go out with the field teams numerous times during both research periods, but the CV ward staff allowed me to simply hang around in the ward, observe the tests and procedures performed on study participants, as well as to chat and ask questions. A similar story could be told of the on-site laboratory staff, the study doctors (I was fortunate enough to be granted a desk in their office from which to base my activities), the drivers, and the administrative staff. Therefore, despite never seeing the beginning or the end of the particular clinical trial in progress, I had as good a perspective of TRO's field office operations as I could possibly have hoped for.

Practice as Data: Following De Certeau's "Walking the City" (in *The Practice of Everyday Life* [1984]), I used 'walking the clinic', that is, my own phenomenological experiences as I inhabited and moved through TRO's field site, as a source of data. Through keeping one eye on these experiences and transformations at all times, I was able to think about how it is that one comes to embody the knowledge-production processes unfolding at TRO's field office and, more generally, how the 'feeling' of the authority of biomedical fact comes to grip the individual as they walk biomedical spaces. Practice, as Bourdieu (1990) would argue, is a key link between the lived experiences of human subjects and the perceived 'objectivity' of biomedical knowledge – and thus I could not but take a rigorously reflexive approach to my research. Granted, in having a doctor as a father and a nurse as a mother, as well as simply inhabiting today's biomedical "macro-colony" (King 2002:773), I was unable to do this from scratch. This no doubt impacted the way I occupied the implicated biomedical spaces. However, before I had any in-depth knowledge of TB, I asked a colleague to perform with me the interview she used for her informants in a related study pertaining to their knowledge of TB (Abney 2011). Since then, I kept a running journal in my field notes of my increasing knowledge of TB as my time with TRO's researchers unfolded.

Interviews: Unstructured and prolonged discussions with TRO's researchers and some other informants yielded many of my most profound findings. These interviews provided great opportunities for us to work together in exploring the day-to-day quirks of what it meant to follow

research protocol, how these took them into highly intimate spaces with their participants, as well as the particularities and consequences of those interactions. It also did not come as a surprise to me to find that some of my informants were better placed academically and intellectually than I to address some of these issues – particularly regarding the epistemological complexities of TB. Indeed, many of TRO's study doctors had been quite widely travelled – both physically and virtually – in the biomedical 'world', allowing me to draw upon a wealth of knowledge and experience in the domain of clinical science on TB. That said, during the first stint of research I did not make enough use of interviews with employees 'lower down' on TRO's payroll – such as the drivers, the field teams, and the study nurses. In the second stint of research I sought, with relative success, to rectify this so as to benefit from a broader range of perspectives.

VI. Ethical Considerations

Generic ethical considerations such as informed consent, protection from harm, and the right to anonymity, whilst crucial, are often inapplicable at the level of abstraction they are commonly discussed (as I have argued at length above). The multiplicity of factors unique to certain types of research and the people with whom they are concerned requires that they be contextualised, amended, and even supplemented with other ethical criteria. Under the following sub-headings I will consider various ethical criteria, some generic, some not, in order that the particularities of my research are adequately brought within the scope of ethical critique.

Bearing Witness: One of the most pressing ethical issues that my research raised was the fact that I was attempting to produce a master's thesis in the midst of often unbearable suffering. On the one hand, I hope that my thesis will have some positive impact on the currently dire situation of TB in South Africa as part of a growing collaborative interest in the disease between my university's Department of Anthropology and School of Public Health and Family Medicine. I have also shared my findings with TRO's researchers, and hope they have found them useful. On the other hand, while I can be fairly sure that my interactions with TRO's participants will help me towards a master's degree in anthropology, I cannot be as sure that TRO's participants, their families or their communities will gain from my research whatsoever. At present, I do not have an answer to this problem, and many anthropologists in similar situations have likewise been at pains to reconcile the socioeconomic inequalities marking the ethnographic encounter. In lieu of such an answer, I attempted to take a lesson from Fiona Ross' work *Bearing Witness* (2002). I endeavoured to bear witness to the suffering of those around me during my research with TRO (some of which is caused by the demands of research protocol), and tried to take it into careful consideration when articulating my findings. In doing so I hope I have at the very least treated these people as not only means to an end (my master's degree), but as ends in themselves.

Informed Consent: During my research I sought informed consent where it was possible from all the people I interacted with. However, what constitutes informed consent, as well as the way in which

this is gathered, is contestable and indeed contested. Of most of TRO's research staff and the other people who participated in my research, I gathered what is to the best of my knowledge verbally informed consent, attempting to ensure at all points throughout my research that they were still comfortable in taking part. Given the sensitive nature of TB (Abney 2011), it was especially important that I remained alert to signs that people are not comfortable taking part in my research. Though this never transpired, if they had shown discomfort in any shape or form related to my research, I would not have included them in my research.

Protection from Harm: 'Harm', much like 'informed consent', is a contestable notion. In the context of my research, I take it to mean any damage, be it psychological or physical, that results from my presence at TRO's field site. I tried my utmost not to cause harm to any of the doctors, nurses, researchers, staff, patients or anyone else I interacted with in the course of my research. There was a very real possibility of TRO's participants and their families feeling alienated as a result of my research. To this end, I refer back to subsection "Bearing Witness" in the hope that this sufficiently alleviates this potential alienation. However, despite the air of objectivity that often permeates biomedical spaces, doctors and researchers are humans too. Thus, I had exactly the same responsibility to TRO and its employees as I did to patients and their families. Good and Good (1993:102) point out, for instance, that when learning social sciences, medical students at Harvard University felt resentment because it brought home a fear that they were losing their humanity in the process of being in-doctor-inated. In doing ethnography at TRO's field site, I was endeavouring to bring out exactly the human-side of science, and as a result I strove to remain sensitive to both my own and biomedical practitioners' positioning when interacting with them, and to protect them from harm accordingly.

Confidentiality: Having had several conversations with TRO's researchers on the matter, I have assigned pseudonyms not only to all staff members and otherwise who feature in the following chapters, but also to the real referent of TRO, to the host hospital, and even to the region of South Africa in which TRO's clinical research takes place. The primary reason for such extensive confidentiality is that TRO strike a delicate balance with the hospital which hosts their endeavours. Especially with my research touching on sensitive ethical issues – in spite of being a largely philosophically oriented piece of research – TRO's researchers were very uncomfortable with my naming (and thus what they feared would be shaming) them. Committed to continuing good relations with TRO, I have happily complied with this wish.

Chapter 2:

An Emergent ‘Trial Community’

I. Introduction

On a bitterly cold morning sometime early in June 2011, I arrived at TRO’s field office for the first time, a large two-story structure on the outskirts of its host hospital’s premises, characterised by the fleet of white branded vehicles lurking in wait outside. There I was welcomed by TRO’s lead study doctor and on-site manager Dr Janssen, and her colleague, Dr Le Roux. I spent my first morning at TRO being shown around the site and making acquaintances with TRO’s trial co-ordinators, quality-assurance (QA) department, drivers, field researchers, laboratory team, and – after a brief walk to the main hospital – the nurses in the CV ward. I was also, to my pleasant surprise, allotted a desk and an internet cable in the doctors’ and co-ordinators’ office, having thought I would be relegated to an obscure corner of the building. In the coming days and weeks, and indeed during my second period of research in June 2012, I was left largely to my own devices, and given a high degree of access to the various facets of TRO’s operations. Although this left me rather at a loss of what to do at first, I quickly – thanks to the helpfulness and cooperation of TRO’s on-site staff – settled into the rhythms of TRO’s day-to-day operations.

The endeavours of the field teams as they travel into the region conducting the follow-up visits and the routines of the CV ward – the points at which TRO’s researchers come into most direct contact with their participants – are the primary foci of this dissertation. However, before ‘following’ protocol into the field and the CV ward (in Chapters 3 and 4, respectively), in this Chapter it is my aim to give a sense of the ‘trial community’ that has been generated by TRO’s operations, and the interrelated factors – involving TB as engaged at different levels of scale, from global discourses to local material contexts – that give it shape. Secondly, in doing so, I hope to provide the necessary points of context for a deeper exploration of the substantive and affective relations at the ‘interface’, which constitute the ‘glue’ that holds the trial community together on the ground. Firstly, I detail the global public health discourses generating the imperative for TB vaccines research. Secondly, I provide some background to the Hareford region and TRO’s engagement therein since 2001 conducting clinical trials. Moving towards the major trial TRO were conducting at the time of my research, I explore the epistemological complexities of researching childhood TB, and how these are grappled with by TRO’s researchers in order to make the disease ‘researchable’. Finally, I provide an overview of

research protocol, designed around TRO's intricate trial 'algorithm', and how this shapes TRO's day-to-day operations.

II. TB Vaccinations Research

Writing in a special issue of *Social Studies of Science*, King (2002) offers an excellent overview of the global structure of biomedical practice and discourse from the colonial to postcolonial era. Before the post-colonial turn, 'public health' – broadly conceived – was steeped in the language of territoriality (i.e. quarantining in, and keeping out health risks from, 'disease-ridden' spaces). However, towards the end of the 20th century, the vastly accelerating flows of people, communication, ideas, commodities – and thus disease – characterising the post-colonial world set in motion a series of transformations in the nature of 'public health' initiatives (2002:773). Rallying around a new 'emerging diseases worldview', exponents of 'public health' turned towards *treating* indigenous populations, so that diseases would not spread beyond control (2002:772). The vision was that through the institution of a "global surveillance network", diseases the world over could be detected, tracked and eliminated with speed and efficiency (2002:774). In Chapter 1, it was noted of the global TB pandemic that there are 8.8 million reported cases, 1.1 million deaths among people who are HIV-negative, and 350,000 among those who are HIV-positive (WHO 2011). In addition, because the conditions under which the disease thrives are prevalent in resource-poor environments, the developing world has 95% of positive diagnoses and 98% of deaths. Given the devastating impact that TB is currently having on the low and middle-income countries, and the possibility of drug resistant strains increasing in number and affecting high-income countries, one would perhaps expect (especially in light of King's [2002] observations) there to be a burgeoning market for the production and mass distribution of TB-related bio-products and technologies.

The reality is less the case. As a number of social scientists have documented extensively, the trajectory of the global market for pharmaceutical bio-products largely follows the trail of profit (Cooper 2008; Fisher 2009; Petryna 2007, 2009; Petryna & Kleinman 2006; Rajan 2006). Unlike drugs and technologies for psychiatric disorders, heart disease, herpes, those related to smoking – and indeed most of those diseases related to lifestyle and old age – the production of drugs and technology related to TB are largely unprofitable from the perspective of large profit-driven pharmaceutical companies (Petryna, Lakoff & Kleinman 2006:2-3). This is because, given the relative impoverishment of the regions of the world with the highest morbidity and mortality rates of TB, governments – South Africa's included – have no choice but to distribute drugs free of charge to citizens with or without health insurance. Indeed, insofar as TB drugs and technologies could be considered 'profitable', it is because effective treatment and prevention could save governments money that would otherwise be spent on keeping patients in hospital wards. As Dr Janssen remarked to me of the current efforts to get TB drugs and technologies on the market, "nobody's going to get rich off this". That said, there are funds being channelled into the limited TB 'market' from primarily

non-profit sources such as the Bill and Melinda Gates Foundation, the Wellcome Trust, and the European-Developing Countries Clinical Trials Partnership. TB shares the attention of these funding bodies with such other diseases of poverty as malaria, pneumonia, and HIV/AIDS. However, institutions engaging TB receive a substantial quantity of resources.

TB is a curable disease and there are a number of first-line drugs (e.g. isoniazid, rifampicin, pyrazinamide) which, when taken in specified regimens over the course of approximately 6 months, should cure afflicted individuals. However, especially in light of the failure of DOTS to prevent the spread of TB in certain high-burden regions, WHO (2012) reports a steadily increasing number of MDR TB cases worldwide (almost 56,000 cases in 2011, up from 46,900 in 2009). Thus it is that one of the priority measures to combat TB has been to concentrate time and resources not only upon the development and distribution of post-diagnostic antibiotics but also on vaccinations to preclude the onset of the disease in the first instance. Professor Helen McShane of the University of Oxford remarked that:

it is important that we continue to develop better drugs and diagnostics to help us rapidly diagnose TB and identify drug-resistant strains, but we must invest in vaccine research now if our ultimate goal is to be able to prevent the disease rather than forever chase growing drug resistance with new drugs (Bizcommunity.com).

The Bacillus Calmette Guerin (BCG) vaccine has served as the only vaccine used on a global scale to prevent TB since its introduction in the former half of the 20th century. It has been widely successful, and has been shown to reduce the risk of pulmonary TB in infants by upwards of 50% on average (although its efficacy is subject to regional variation [Colditz, Brewer & Berkely 1994]). However, it is widely thought, especially given the continuing proliferation of drug-resistant strains of the disease, to be insufficient as a self-standing TB preventative. Thus, the goal at present is the production of a supplementary booster vaccine which will increase the overall efficacy of the BCG, and to provide a more comprehensive protection against the disease in its multiple manifestations. The successful production of this vaccine, as was the case of the BCG, is an expensive goal, requiring not only multiple stages of pre-clinical innovation and experimentation, as well as a host of clinical trials in high prevalence regions to test both its safety and efficacy on a large scale, but also an estimated 200 million US dollars to fund the endeavour. In sum, in the context of the fight against a disease for which funding is a major challenge, the production of the much needed booster vaccine for the BCG will be no mean feat.

III. TRO and the Hareford Region

Established in 2001, TRO has for over a decade been in the important endeavour to develop and advance TB vaccines, particularly with their extensive clinical trials in the Hareford region of South

Africa. The Hareford region is a primarily agricultural enclave with a population of around 850,000, located approximately 120km outside of a large city. It has a proliferate economy compared to other regions which is grounded in the produce of its multitude of wine farms, constituting approximately 10% of the country's GDP. Despite the proliferate rural economy in the region, like many parts of South Africa the Hareford region remains haunted by a legacy of apartheid governance which has left the majority of wealth in the hands of the few and the vast majority in poverty. On the one hand, South Africa's race-based health system (comprised of 14 separate health departments in 1994), which systematically deprived those labelled non-white people of adequate healthcare during apartheid, has been dismantled. Over the last decade or so, under a now-unified and non-segregated health system, the public health sector has undergone a series of major structural changes in order to make adequate healthcare more equitable and accessible. Certain areas of the Hareford region have experienced particularly positive improvements in the provision of primary healthcare (TRO 2012). On the other hand, high levels of chronic poverty remain. De Toit (2004:991) notes that in farming regions of the country, workers are subjected to grim living conditions, do back-breaking labour, and receive very low wages. To make matters worse, a consistent income has become even less dependable in the wake of the farming community having moved towards hiring seasonal workers rather than employing workers full-time⁴. Thus, while primary healthcare facilities have improved, the burden of disease and premature mortality remain high.

The leading cause of premature mortality in the Hareford region in 2006 was HIV/AIDS, although in the context of a dire problem of alcoholism in the region (a legacy of the 'dop' system of payment on wine farms during apartheid⁵ [Levine 2011]), the leading cause of premature mortality among men was homicide (Hareford Regional Office 2008). The second overall cause of premature mortality among both men and women in the region, meanwhile, was TB disease (accounting for 11% of the total). In 2006, the province in which the Hareford region is located was reported to have the highest number of new smear-positive cases of the disease in the country (518 per 100,000). Hatherill et al. (2011), moreover, estimate that the number of new cases of TB in children 0-2 years of age was upwards of 300 per 100,000. It is largely unclear exactly why it is that, in spite of the comparatively successful primary healthcare system in the province, the burden of TB disease is so drastically high. However, it is not a completely unsurprising finding. With a co-infection rate with HIV and AIDS rate of approximately 30%, cramped and often unsanitary living conditions, high levels of alcoholism, and regular exposure to agricultural pesticides, there is certainly cause for speculation. In response to

⁴ Following strikes in the mining and manufacturing industry, there has been an insurgence of strikes among farm workers, particularly seasonal workers, demanding higher wages (from around R60 to R150 per day) and improved living conditions. The minimum wage has been raised to R105; it has been reported that farmers will have to cut back on unskilled labour.

⁵ The 'dop' system entailed payment partially in alcohol rather than money, which resulted in devastating rates of alcoholism among workers on wine farms during apartheid. Although the dop system has been dismantled and criminalised, alcoholism rates remain extremely high.

this, the province's Department of Health has intensified its response to the epidemic as of 2006, in particular the quality of their DOTS implementation, under the heading of the "Advanced TB Response Strategy".

TRO began its activities in the Hareford region under the name "The BCG Trial Group". It was named after the organisation's initial purpose of conducting clinical trials into the efficacy of the BCG vaccine against childhood TB, an endeavour that required a relatively stable trial population, a high burden of TB, and well-functioning primary healthcare facilities. The Hareford region fitted these criteria. The BCG Trial Group's research activities were to encompass approximately 400,000km² in the region, and the approximately 350,000 people living in that catchment area. In the early stages of the site's development, TRO's researchers engaged the 'general public' in the region by advertising (using the local media) a public meeting in a restaurant which would provide a broad overview of TRO's nature and intentions (in particular "the BCG trial", as it was popularly known). That initial meeting and the ones that followed (which took place in various locations, including a library and city hall) marked the beginnings of what is now a regularly scheduled meeting between TRO and its 'Community Advisory Board'. The BCG (phase IV) clinical trial quickly got underway, and TRO (then still the 'BCG Trial Group') were able to enlist almost 12,000 infants in pre-natal clinics around the region over a period of 3.5 years. So successful were TRO in this regard that the human resources required to run such a big trial largely outstripped what had been anticipated. Consequentially, TRO's original team were forced to hire several other researchers to keep the trial running, including a number on the host hospital's payroll. This first clinical trial, and the institutional expansion it necessitated, proved to be the vital stepping stone for "developing the infrastructure and capacity to conduct large-scale TB vaccine trials" (TRO 2012).

In the intervening time between the first BCG clinical trial (which ran for approximately 4 years) and the present day, TRO have undertaken a number of clinical trials which vary in nature and scope. TRO's name-change from the 'BCG Trial Group' reflected the shifting impetus of the organisation's endeavours from conducting phase IV trials on the current BCG vaccine to trialling the safety and efficacy of booster vaccine candidates for the BCG (see the preceding section). Over the last few years, TRO have conducted clinical trials on five booster vaccine candidates in the context of eleven different protocols. Although during 'the BCG trial' TRO only had the capacity to conduct one trial at a time, they now have the capacity to conduct a number of trials concurrently, in addition to studies on such important issues as "novel approaches to informed consent, tools to measure the tuberculin skin test, approaches to diagnosing TB disease in children for late-phase vaccine trials, and detailed studies of the vaccination-induced immune response" (TRO 2012). In order to support these wide-ranging research interests, TRO's personnel has grown to more than 190 people over a ten year period (many hired from around the Hareford region), and its funding is now in excess of R50 million per annum. But none of this would have been possible were it not for the co-operation of 20,000 plus people in the Hareford region who have participated in their studies over the last ten years or so (5.7%

of TRO's catchment population, and 2.5% of the region's total population). In sum, TRO has a well-established existence in the region, and a relationship with the communities in the region that is greater than the sum of its individual clinical trials.

IV. Trialling a BCG Booster Vaccine

TRO's largest current study, one which is also being conducted at a number of other research localities around the world, is a phase IIb clinical trial designed to determine the safety and efficacy of a particular booster vaccine for the BCG. By the time that I arrived at TRO's field project office in June 2011, the study was already two years underway: infants had been enrolled into the study, the trial vaccine had been administered, and TRO's researchers were busy monitoring the condition of participants to determine if any were developing TB disease or if the vaccine was causing any 'adverse effects'. There was an air of routine busyness to the place. After spending time out with one of the field teams and with the nurses in the CV ward, and conversing with Dr Janssen and Dr Le Roux, I began to get a sense of the extent of the demands of trialling a TB vaccine in practice. As a result, in spite of a rough and ready understanding of TB, I felt unable to attribute much significance to what was going on before I had acquired a better understanding of TB as a disease entity. It transpired that TB – and childhood TB in particular – is an extremely complex disease to diagnose and thus research, and the ways in which these complexities are grappled with play a large part in shaping the particularly intimate nature of the day-to-day requirements of protocol. And those intimacies play a large part in binding TRO and its participants in a 'trial community'. Thus, before detailing the particularities of the trial's protocol (in part ii of this section), I would like to discuss how TB is engaged at TRO.

i. Diagnosing Childhood TB in a Clinical Trial

TB is an often fatal infectious disease that is caused by the agent *mycobacterium tuberculosis* (henceforth *M. Tuberculosis*). The disease usually – in its pulmonary form – attacks the lungs, though also often impacts other parts of the human constitution such as the spine, the groin, and the brain. In terms of how it is spread, it is a primarily airborne disease that is transported via sputum when people with TB cough, sneeze or otherwise transmit the body fluid to one another. Talking to Dr Janssen one morning, she explained to me that the tools and techniques for diagnosing the disease have remained remarkably constant over the last 50 years:

In the end, it [diagnosing TB] hasn't changed that much from what we were doing 50 years ago, you know, you've got your classic signs and symptoms, plus or minus an X-Ray, plus or minus a Mantoux skin test...and the ultimate gold standard is a positive culture...The only addition is something like a quantiFERON test, this new test, but it's certainly not allowed to stand on its own.

Let me clarify Dr. Janssen's remarks. The main techniques used to identify 'latent' TB disease are the Mantoux skin test and the quantiFERON blood test, both of which are designed to trigger immunological responses which signal *M. Tuberculosis*. The techniques used in addition in order to identify 'active' TB disease are spotting clinical symptoms, reading chest X-rays, and performing sputum smears and cultures. The most common clinical signs and symptoms in children are: weight loss, failure to sufficiently gain weight, a chronic cough, night sweats, a high fever, and a failure to respond to antibiotics. Chest X-ray's meanwhile are used to identify 'TB cavities' or any one of a number of other manifestations of the disease in a person's lungs. Sputum cultures are particularly noteworthy. TRO's researchers – and the biomedical world more broadly – generally refer to it as the diagnostic 'gold standard'. It involves collecting a sample of sputum from a body suspected of having TB disease, before applying a compound designed to 'stain' the microorganism and thus render it visible to the gaze of the laboratory technician examining the sample under a microscope (IUATL, 2000). This allows laboratory technicians not only to determine with a much higher degree of certainty whether a patient has 'active' TB, but also allows them to discern the particularities of the *M. Tuberculosis* strain and, importantly, if it is resistant to any antibiotics.

Unfortunately, TRO – like many TB research initiatives – is not able to benefit from the certainty afforded by the culturing of sputum samples. The sputum culture was coined the diagnostic 'gold standard' because of its success in diagnosing HIV-negative adults, who, if they have TB disease, generally carry a high quantity of *M. Tuberculosis* bacteria in their sputum. However, in the case of HIV-positive adults, infants and younger children – the latter two being the particular concerns of TRO's trial – the *M. Tuberculosis* bacteria are not particularly prevalent in their sputum. The majority of the bacteria reside in more enclosed regions of the lungs. Consequentially, as Dr Janssen explained to me, in infants and children sputum cultures only identify instances of TB disease approximately 25% of the time. While this still makes it a powerful diagnostic tool, it is not the 'gold standard' it is when used on HIV-negative adults. To make matters even more difficult, while adults – both HIV-negative and HIV-positive – are usually able to cough on demand and sputum has to be procured from infants' lungs by using either a 'sputum induction' or a 'gastric lavage' (see chapter 4). These are time and resource intensive processes, rendering sputum not nearly as efficient a diagnostic tool for children as it is in adults. TRO's researchers thus have a number of diagnostic techniques at their disposal by which to make diagnoses of TB, but none which are individually sufficient to make correct positive diagnoses.

In the absence of a gold standard, moreover, there is no single manifestation of the disease that is displayed by, and cuts across, all afflicted bodies. Therefore as far as anybody can actually *know* a particular child may have TB disease, and yet only display a small number of the signs and symptoms associated with TB. Given this state of affairs, the diagnoses of TB disease made by different biomedical practitioners across time and space have a tendency to diverge as they accord different weighting to various signs and symptoms (Hatherill et al 2009:314). Dr Janssen, in one particularly

memorable turn of phrase, said that “it’s as though it doesn’t exist. Not quite, but...” Although Dr Janssen was being slightly ironic, childhood TB is an undoubtedly elusive disease. The problem with this for the conduct of clinical research on childhood TB is that, while this may be acceptable in a clinical/treatment-oriented context (see Chapter 4), it threatens the prospects for the production of the kind of high quality clinical data required by the Medicines Control Council (MCC) – South Africa’s primary regulatory body – and FDA when trialling vaccines. In particular, it threatens the prospects for a consistent independent variable (means of diagnosing TB) against which to measure the dependent variable (incidence of ‘active’ TB disease). Dr Janssen thus argued that it is of utmost importance to clearly ‘define’ childhood TB disease in the context of vaccines clinical research:

There's not a blood test you can do and there's not one single X-Ray you can hold up and say yes its TB, so for any vaccine trial where your outcome is TB you've got to know that you're all calling the same thing TB...you've got to define what you're going to call TB, otherwise it could affect the whole future of your vaccine.

The challenge, then, is to define childhood TB in a certain way so as to make it transportable, comparable, and ultimately researchable in today’s tightly policed bio-scientific world – to make it an “immutable mobile”, to borrow Latour’s (1987) phrase. In other words, the challenge is to render TB compatible with the ‘ordered separations’ that give clinical trials epistemic authority in today’s tightly regulated and mobile biomedical world.

The means by which childhood TB is ‘defined’ and thus rendered an ‘objective’ disease entity is via what are known as diagnostic ‘algorithms’. These work by taking as inputs various clinical (e.g. weight loss, chronic cough), radiological (e.g. cavities on an X-ray) and immunological (e.g. Mantoux, quantiFERON tests, sputum culture) signs and symptoms displayed by infants, and giving as outputs a value which aggregates the values of the various inputs. The output – paradigmatically, either a positive or negative diagnosis of childhood TB – will usually reflect the capacity of the signs and symptoms displayed by an infant to fall under a range of different types of signs and symptoms – clinical, immunological, radiological etc. The virtue of using diagnostic algorithms is that clinical researchers can use a single, consistent, overarching diagnostic tool (i.e. the algorithm) to assert with a high degree of accuracy, for a great number of infants with a great number of diverging signs and symptoms, whether or not they have TB disease. Indeed, it allows for a degree of standardisation not only within but also *between* research contexts in the interests of comparing and contrasting clinical data (cf. Simpson & Sariola 2012:565) TRO is therefore able to produce clinical data which is comparable with that produced in the context of research into other diseases, and thus has the capacity to meet the standards enforced by the MCC and FDA.

ii. Trial Protocol

In the above paragraphs I pointed towards the epistemological complexities of diagnosing TB in children and argued that, through the use of algorithms, childhood TB has been rendered a researchable disease entity. Nonetheless, acquiring the multiplicity of input data required to run the trial algorithm on a large scale – and thus to measure the efficacy of a vaccine – is a challenging pragmatic exercise. Thus, although one of the primary goals of TRO's current study is to determine the safety of the trial vaccine, the study protocol is given shape largely by the various processes required to run the diagnostic algorithm for every infant enrolled in the trial. Paradoxically, having childhood TB compatible with the 'ordered separations' of medical research, the resulting trial protocol within which it is implanted entails frequent interactions with participants and the constituents of the Hareford region. The protocol is, like the algorithm it enacts, designed to be 'objective' and 'detached'; but in practice it entails the relational-affective practices that are the focus of chapters 3 and 4. Below is an overview of trial protocol, which will be developed in greater detail in the following chapters.

True to the 'gold standard' clinical trial, TRO's current phase IIb (safety and early efficacy) study is a double-blind randomised control trial: some of the participants were given the trial vaccine and the others were not, wherein neither the participants nor TRO's researchers (except in exceptional circumstances) know which participants had been given what. Over a two year period (starting in 2008), TRO's researchers visited clinics around the Hareford region as infants were having their routine immunizations administered. With the written 'informed consent' of mothers, TRO's researchers enrolled into the study just shy of 2800 infants between the age of 126 and 182 days without either HIV or TB infection. After receiving the trial vaccine (or, if they were in the control group, an approved alternative), the infants are 'followed up' at day 7, day 28, day 84, and every 84 days from then on in for two years after enrolment. This is in the interests of detecting signs that they are developing either TB disease or any other 'adverse effects'. The 'follow-up' visits are scheduled to take place at the infants' homes, and thus teams of field researchers head out into the Hareford region each day to locate a specified number of infants. During each visit, in order to assess the wellbeing of the participant the field teams are prescribed a series of questions to ask of the mother regarding the participant's health, and must also weigh the infant itself to determine if they are losing or inadequately gaining weight (more about that in Chapter 3). If they cannot locate the infants on the specified day, there is a five-day window within which they can try to find them without compromising the 'integrity' of the study.

If reason is found during the 'home visits' that a participant might have developed TB disease (e.g. weight loss, chronic cough, positive Mantoux skin test, contact with a TB-infected adult), one of TRO's study doctors is tasked with the decision to bring them into the Case Verification (CV) ward on for further tests and examinations. Informing the participants' mothers (or close relative) that they need to bring the infant in to the CV ward, meanwhile, as well as negotiating the best possible date to

come in, falls to the follow-up teams. When they bring the participant in on the specified date, the infant is subjected to a tightly scheduled series of tests and examinations which take place over a 48 hour period. Among other things, this involves a diagnosis of TB, made independently of the trial itself, which is performed by a clinical doctor for the purposes of potential treatment (more about this in Chapter 4). After the 48 hours, provided the participant does not have TB the infant is discharged and can go home – though if reason is found during subsequent home visits they may be brought back in to repeat the process. Throughout the duration of the trial, the information required to run the algorithm for each enrolled infant, as well as any relevant information as to the safety of the trial vaccine (e.g. any observed ‘adverse events’), is uploaded onto a computer database. At the end of the trial an output for the algorithm will be computed for each infant, and all other data will be analysed, in order to confirm or disconfirm the safety and efficacy of the trial vaccine.

V. Conclusion

Through an exploration of TRO’s operations to the present day, I have demonstrated that TRO’s engagements in the Hareford region since 2001, which has included more than eleven different studies and upwards of 20,000 participants, warrants a more grounded and nuanced perspective on its operations than is suggested by the prevalent narrow conception of clinical trials. Like a number of anthropologists involved in the study of the interface between global medical research structures and particular localities of clinical research (Geissler et al 2008; Gikonyo et al 2008; Kelly 2011; Leach & Fairhead 2011), I therefore urge that we view TRO and the people of the region as constituents of an emergent ‘trial community’. However, what I have begun to argue in this chapter – an argument that will only be complete with the addition of the arguments of the following chapters – is that this ‘trial community’ is inseparable from TB as complex disease entity and socio-historical phenomenon. The work that this particular chapter has done to this end is to demonstrate that TRO’s ‘trial community’ has been generated, and given its particular ‘shape’, by the global imperative to trial prospective booster vaccines in high prevalence localities such as the Hareford region, the appropriation of an ‘objective’ trial algorithm to render childhood TB researchable, and the resulting frequent and intimate interactions that punctuate day-to-day trial protocol. This shall serve as the necessary counterpoint for exploring the interface between the ‘ordered separations’ of bio-scientific methodologies (embodied in trial protocol) and the relational-affective dimension of TRO’s current trial in the context of the follow-up visits (Chapter 3) and the CV ward (Chapter 4).

Chapter 3:

The Follow-Up Teams at the ‘Interface’

I. Introduction

In the preceding chapter, I demonstrated that the structure of TRO’s trial protocol is largely determined by the epistemological complexities of diagnosing childhood TB: even though the disease has been ‘separated’ from relations via the appropriation of an algorithm, a complex and intimate pattern of interactions is required to procure its inputs. The following two chapters are situated at the ‘interface’ of the global research structures (embodied in trial protocol) and the socio-economic reality of the Hareford region, where an implicit relational-affective dimension (the ‘glue’ that holds ‘trial communities’ together) permeates day-to-day research. In this chapter, through ‘following’ protocol as it takes TRO’s field teams into the Hareford region to conduct the follow-up visits, I demonstrate that completing the requirements of protocol necessitates a dexterous disposition and intimate knowledge of the social dynamics of the region. I then explore the dynamics of and interrelations between separations and relations, protocol and ‘extra-protocol’, as the follow-up visits are used as an opportunity to screen for the non-TB-related medical problems. Finally, I explore how TRO grapples with the sensitive issues of physical abuse and neglect, which are prevalent phenomena in the region. I conclude by concurring with Geissler and Molyneux (2008:688) that fieldworkers be acknowledged as playing a vital and under-acknowledged role in ‘making clinical science work’. However, I urge that the challenges they face on the ground be understood in particular epistemological context related to TB research and its inseparability from the fraught landscape and history of the Hareford region.

II. Establishing Contact

An integral part of TRO’s current research protocol is conducting the follow-up visits. As I pointed out in Chapter 2, the purpose of the follow-up visits is to determine whether any of the infants enrolled in the clinical trial are showing signs that they may be developing TB or any ‘adverse events’, the former of which entails a visit to the CV ward for further tests and examinations. Performing the follow-up visits is not an easy task. With 2800 infants having been enrolled into the clinical trial over a staggered time period of nearly two years, several teams of field researchers – coordinated by a number of administrative staff – drive out into the Hareford region each day to locate a specified number of participants (upwards of 10 during busy times). Each team is comprised of at

least two members: a driver, who is responsible for the car and for locating the homes of TRO's participants; and another field researcher, who is in charge of conducting the requirements of the follow-up visits themselves. A third team member is often included to make the process run more smoothly. Wanting to see firsthand what the home visits entailed, one morning I entered the follow-up visit teams' office space before they were due to leave, hoping to find a team who would allow me to venture out with them that day. Fortunately, I found myself only ten minutes later heading out of the hospital's premises with Yolanda and Lucinda – a team which sometimes includes Digby – in one of TRO's vehicles. Their operations encompassed primarily farming communities (though some of the other teams have a more urban participant-base). In this section, I emphasise the dependence of conducting 'objective' clinical research on the intimate knowledge of the region and its constituents held by the follow-up team, and the dexterous practices they must adopt to complete the (abstract and a priori) requirements of protocol.

One of the first things which struck me in my first few days with Yolanda and Lucinda was just how difficult and unpredictable the daily life of one of TRO's field researchers can be. As Yolanda mentioned to me, partially in warning, before we had even made it out of the hospital premises on my first day, "when you leave the office you don't know what's going to happen – you only know when you get there". The complexities start with locating TRO's study participants. On the way to one of the farms, Yolanda explained to me that the constituents of the Hareford region are highly mobile, with increasing numbers of farm workers being hired on a seasonal basis, forcing them to move around depending upon availability of work (see also Chapter 2). Therefore the mothers of TRO's participants are known to move homes frequently, and sometimes at quite some distance from their last location. The infants' mothers were, on the one hand, asked to provide a cell-phone number at the beginning of the study in order that they could be located easily. However, often changing their cell-phone numbers without alerting TRO, they can be incredibly hard to locate. This is made all the more problematic by the fact that farmers – not entirely trustful of TRO's intentions with their workers, as a number of TRO's researchers pointed out – can make finding participants very difficult. Allow me to give one memorable example.

As I mentioned in Chapter 2, if the decision is made that a participant needs to be admitted to the CV ward to determine whether they have TB, it falls to the follow-up teams to alert the mother. One morning, we were trying to make contact with a particular mother whose child who was thought to be showing signs of TB, and thus needed to come for further tests. Lucinda, after her attempted cell-phone call went "straight to voicemail", concluded that this mother had changed number. Accordingly, we drove out to the farm on which she was believed to live in the hope that contact could be made with her that way (and that her new contact details could be obtained). We drove into the farm along a bumpy mud track, before pulling up outside her house. Lucinda knocked on her door, but nobody answered; nor did there seem to be anybody else around – another farm worker for instance – to ask as to her whereabouts. Making our way back down the track, we encountered a

farmer driving his tractor in the opposite direction. Yolanda asked him as to the location of the woman in question, to which he responded brusquely that she no longer worked on this farm and that we should try elsewhere. Perplexed, Yolanda asked us as we drove out of the farm, “are we talking about the same person?” After stating that “something’s not right”, Yolanda decided that we should visit the farm again after lunch, so we went about tracking down other participants in the meantime. Sure enough, after returning to the mother’s house after lunch, we found her in her front yard talking with a neighbour. Lucinda alerted her that her child needed to come into the CV ward for further tests, negotiated a date with her, and then we were on our way.

Whether the farmer was deliberately undermining the team’s attempt to establish contact with the mother it is impossible to determine. However, without Yolanda’s ‘gut feeling’ that something was not right, a feeling borne of experience, we would have spent far more time searching for her. But even in the instances when the whereabouts of the mothers and infants are known, the visits are often far from easy to conduct. Ideally, the site of the visit is the infants’ homes, because those are the locations which TRO – in theory, at least – have on file, and also because they usually afford a degree of discretion. More often than not, however, the visit falls during working hours, when participants’ mothers are labouring along the grapevines. Therefore, while I was with Yolanda and Lucinda, the follow-up visits had to be conducted in two stages in often completely *ad hoc* locations (I will discuss the specifics of follow-up visit protocol below). Firstly, after tracking down the mothers along the grapevines (which usually required asking directions of two or three people), Yolanda or Lucinda would ask various questions of the mothers through the car window, or, if possible, with the mothers seated in the back of the vehicle. Secondly, we had to drive to another location to examine the infants themselves, who were usually to be found at a “crèche”⁶ on the farm, or, less often, with another relative nearby. Once there, the crèche leader – and occasionally, the mother, if she had the time to join us at the crèche – assisted the team with examining the infants. Sometimes we would have access to a side room; but as often as not, the whole follow-up visit process had to be conducted in the communal space in front of the other infants.

It is noteworthy that the role that TRO’s field teams occupy in the ground-level conduct of clinical research, locating and ‘following-up’ participants, is somewhat different in nature than the fieldworker roles accorded a high degree of importance in other ethnographies of trial communities (Geissler et al 2008; Gikonyo et al 2008 Molyneux & Geissler 2008: 692). Fieldworkers employed by the MRC in The Gambia during a large malaria vaccine trial (MVT), for instance, lived within the study population for the duration of the trial. For every “village household” was employed one field worker and one nurse, who lived under and subsisted with that household (Geissler et al 2008: 701). Playing a vital role building trust in the MRC, and continuously communicating with participants

⁶ The farm “crèches”, labelled as such by the field team, are very different from the urban-based, tightly regulated institutions that usually fall under the name. The ones I encountered were usually small, with many infants, few staff, and little in the way of resources.

about the nature of the trial, fieldworkers claimed to take pride in building relationships with “their group” through the duration of the trial (Leach & Fairhead 2011: 83). This level of intimacy with participants is not possible for TRO’s fieldworkers, who, with more participants spread over a far greater distance to ‘follow-up’, are only able to engage with participants and their families for comparatively brief, intermittent periods. Nonetheless, I would strongly contend that their dexterous practices embody just as greater relational knowledge – as opposed to knowledge *about* people, as per the representational knowledge sought after in clinical trials – as the MRC fieldworkers (Whyte 2011:37-40). Largely unacknowledged at the abstract level of trial protocol, the challenges the TRO’s follow-up teams face in the region on a day-to-day basis and the dexterity required to overcome them “do not show up on paper”, as Yolanda tellingly put it.

In any case, after over twelve years of conducting clinical trials on over 20,000 participants, TRO is well-known in the Hareford region and treated with a degree of familiarity consistent with the notion of ‘trial community’. As we drove through various settlements and farms, neither the branded vehicle nor the follow-up team received more than a passing glance, and the few we received were usually cast in my direction, which suggested that it was only because I was not a recognised member of the follow-up team. Upon asking Yolanda about this, she said that it took a number of years before the people in the region were accustomed to the presence of TRO’s vehicles. However, years later, they are now such a familiar sight in the communities that they have now picked up the nick-name “the TB people”. Indeed, during a cell-phone call only minutes later, before Yolanda had even introduced herself came the shout, “Abigail, it’s the TB people” (cf. Kelly 2011:230). Perhaps as a result of the long-standing presence in the Hareford region, an air of routine permeated the interactions with infants’ mothers or relatives as we made our way through the daily lists of participants to follow up. After meeting TRO’s vehicles outside their homes (when they were at home, that is), they were prompt and, seemingly unhesitant, about allowing Yolanda and Lucinda into their homes and to physically examine their children. Often routine formalities would extend into more personal discussions about the ins-and-outs of their day-to-day lives. These exchanges betrayed a degree of intimacy which I had not expected to see in the middle of what is, after all, a bio-scientific experiment. But of course, anthropologists of ‘trial communities’ contend, such intimacies are the essence of clinical research on the ground.

III. Completing the ‘Form’

Nonetheless, all parties – even the infants, from the distressed expressions they often wore – were aware of what a visit from the follow-up team meant. As I mentioned in the previous chapter, the purpose of the visit is to determine whether the participant is showing any signs of TB or any ‘adverse events’ that might be causally related to the trial vaccine. This entails looking for certain signs or symptoms, as well as weighing the infant to determine if they are losing or inadequately gaining weight. Guiding this task is the follow-up visit ‘form’, the completion of which is mandatory insofar

as the trial protocol is concerned. The form is comprised of a series of questions to be asked and boxes to be ticked, the majority of which are completed on the basis of the testimony offered by the participant's mother or other relative. Questions include whether the infant has a chronic cough, if they are experiencing a high fever, if they have had a positive Mantoux skin test (for latent TB) at a clinic, if they have been in contact with any TB-positive adults, if they have been treated for any illnesses, and whether they have been taking any particular medicines. There are also some pragmatically oriented questions, such as how many attempts it took to locate the participant, the relation of the carer to the infant, and whether their cell-phone number or address have changed since the last follow-up visit.

Perhaps the most characteristic feature of the follow-up visits – and certainly the most difficult to accomplish – is weighing the participants. Keeping accurate track of each participant's weight is important, because weight loss and insufficient weight gain are some of the most telling clinical signs of childhood TB (see Chapter 4). This has to be performed while the infants are naked, because the added and varied weight of an infant's clothes, no matter how apparently insignificant, can distort the 'reliability' of the reading. However, likely because of the break from routine, the scales used to procure a weight-reading, and the presence of strange people making contact with them, this is a highly distressing affair for the infants. At one participant's home, it took a number of attempts to persuade an increasingly distraught infant to stand on the pair of scales for the length of time required to get an accurate reading. But even then, the infant would not stand still on the scales, and thus had to be placed in a bowl added to the scales – one generally used for infants not yet able to stand of their own accord – to get the desired effect. In another participant's home, they were also completely unwilling to stand on the scales for a sufficient length of time. In the absence of the bowl that day, the participant's mother had to be weighed once, and then again with the child in her arms, with the child's weight deduced from the difference. Barely a day went by while I was out with the team where weighing participants was simple.

IV. Beyond the 'Form': The Provision of Healthcare

Completing the 'form' is, in effect, all that is required of the follow-up teams by trial protocol. True to the 'mechanical' or 'regulatory' objectivity required for production of viable clinical data for the purposes of the trial (Simpson & Sariola 2012:565), the follow-up teams are implored to do so with as minimal degree of interpretation as possible (within reasonable parameters). Dr Le Roux explained to me that:

...we set certain thresholds of interpretation, like "cough for two weeks", which is an indicator that they need to come in [to the CV ward], but we don't want them going any further than this – we want *less* interpretation.

Similarly, Lucinda said to me that “the sisters and doctors know better than we do. We just provide them the information”. Given this impetus, it is fitting that the challenges faced by the follow-up teams are not recognised; what shows up ‘on paper’ is clean, un-interpreted data upon which subsequent decisions can be made. However, having sat in on one of the “TB Reviews” back at the field office – a weekly seminar that all of TRO’s follow-up teams are advised to attend, run by Dr van Zyl – I knew that the field teams are also encouraged to take a “holistic” perspective regarding study participants that transcends the barest requirements of the form itself. This second “holistic” requirement is quite at odds with the protocol-sanctioned form of knowledge production, in practice entailing quite a high degree of interpretation. This means looking out for relevant contextual factors, such as whether they live in proximity to a sewer, if they look under or malnourished, if they have foetal-alcohol syndrome – even whether they are currently teething⁷. This also importantly includes listening for subtleties of speech, in and between the questions prescribed by the form, which might signal medical problems.

To an extent, looking out for these often subtle points of context is ‘relevant’ to the clinical trial itself. For instance, teething, malnutrition and foetal alcohol syndrome can cause an infant to struggle with weight and in a manner not necessarily related to TB. Thus, if these can be flagged early on, there may be reason to spare the infant and mother the discomfort and inconvenience of having to attend the CV ward for extensive tests and examinations (this point will be revisited in Chapter 4). In addition, given that the current study is primarily to determine the safety of the trial vaccine, it is especially important that all medical matters and additional observations be taken into consideration lest they be causally related to the vaccine. However, another reason for maintaining a holistic, context-specific awareness is that the intimacies entailed by the follow-up visits yield opportunities to provide healthcare for participants that their mothers might not have access to or ask for otherwise. Although a view shared by TRO’s other on-site study doctors, it was Dr van Zyl who advocated this approach most vocally:

What I was trying to implore them to do [in the TB Review] was to look beyond what they have to look for, because even though they’re over to screen for TB and that sort of thing ... sometimes some of these kids might not get seen by someone with some sort of medical background ... If there are other things to identify, I’d like them to use it as an opportunity to screen for other things too – I’m sure Johan and Chrizane would agree as well ... It’s so important that any time they have contact with anyone who has some insight into healthcare and links to resources that these opportunities get used as far as they possibly can.

⁷ Both teething and foetal-alcohol syndrome can cause weight loss or insufficient weight gain. The latter is a tragically common occurrence in the Hareford region, directly related to the high rates of alcoholism in the wake of the ‘dop’ system.

The ‘holistically’-trained gaze that TRO’s study doctors are attempting to foster in the field teams is akin to that of a clinician, one sensitive to precisely the often subtle signs, symptoms, and relations between them that might betray a medical problem. In this sense, the doctors are fostering in the field teams the gaze that *they* would bring to bear on participants were they conducting the follow-up visits, using the field teams as ‘eyes’ in the field. Attention has been brought to the “distance” that has been brought between clinical doctors and their patients as a consequence of the blinding procedures entailed by clinical trials (Easter et al 2006; Mueller 1997; Simpson & Sariola 2012). Here we see something slightly different. In the context of an effort to provide healthcare that transgresses into ‘extra-protocol’ terrain, a clinical gaze – and a doctor-patient relationship of sorts – is being projected at quite considerable – spatial – distance across the Hareford region through the mobility of the follow-up teams as they conduct the follow-up visits. The means by which this practice is converted to treatment outcomes is that, in the event that the teams identify a potential medical problem – even if not related to the vaccine – it is reported back to TRO’s study doctors or nurses (immediately via cell-phone if necessary). From there, an arrangement is usually made with one of the local clinics to provide treatment. Similar to the findings of other anthropologists of trial communities (Geissler et al 2008; Gikonyo et al 2008; Kelly 2011; Leach & Fairhead 2011), then, the mobility of TRO through the conduct of the follow-up visits makes the organisation a small but important part of the therapeutic landscape of the Hareford region, creating both new tethers to healthcare resources for its constituents, and, in the process, the substantive relations and material transactions in which ‘trial communities’ on the ground consist.

However, a number of TRO’s researchers believe that while this mode of healthcare provision has many successful outcomes, it is not so easy in practice for the follow-up teams to pick up on the often subtle signs that a participant is in need of healthcare. Therefore the capacity for TRO to contribute to the provision of healthcare beyond the requirements of the trial is not as strong as it could be. Head of TRO’s on-site quality assurance team, Yvonne, explained to me that this is largely because of a lack of professional medical training:

You’re sending field workers with no medical background into a situation to use an algorithm ... or a questionnaire, yes/no, ask a question, get an answer. The challenge is ... you ask the question, and the *human* that’s sitting in front of you in this situation in the environment they are in, they see this as an opportunity to discuss things, or to find help, and they’re dealing with someone who can’t help them, who doesn’t have the insight to pick up the hints or the medical information that is given in those few sentences, for them to make an informed decision and answer ... so I think they’re struggling.

While TRO’s field teams are in the process of receiving training by the quality assurance team in order to improve their sensitivity to medical problems – of which the ‘TB reviews’ are a component – it is currently beyond the scope of TRO’s resources to send out ‘trained’ medical professionals into

the Hareford region. That said, from their research in under-resourced HIV testing facilities in East Africa, Hardon et al. (2011:196) note that “the dynamics of care ... are shaped by the specificities of the care provided” and “professional training and human resource constraints.” Although unable to offer the ideal degree of medical expertise, while I was out with Yolanda and Lucinda conducting the follow-up visits – and through subsequent discussions with other field teams – I began to acknowledge the ways in which they compensate for a lack of formal training. In addition to reporting back to the field office with information that might signal matters of medical concern, the field teams are able to identify when certain ‘home remedies’ are not working, recommend when it is a good idea to visit a local clinic and offering to drive participants and their mothers for health-related purposes when it would be difficult to make the journey otherwise.

The usefulness of TRO’s vehicles is particularly important, and demands an example. To keep warm, especially in winter, open fires are often built in metal bins. Visiting a participant at a crèche on one of the farms, Lucinda and Yolanda saw that the infant had a burn on her right arm from touching one of the bins, and was complaining to the crèche caregiver that she was in pain (“they’re two years old now and can say when they’re uncomfortable” – Lucinda). The only information that the caregiver could provide was that the participant’s mother had not taken her to the clinic. Not wanting to leave the child in pain, Lucinda called the mother on her cell-phone to find out the story. As it transpired, it was going to be another full week before the mobile clinic was due to visit the farm, and the mother was afraid of the dangerous hitch-hike back from the clinic in the nearby town late at night (a clinic visit can take all day). Thus, Lucinda and Yolanda made arrangements with the farm manager to take the infant and mother to the clinic and back, which was accomplished far more quickly, efficiently, and safely than might have been the case. For the most part these ‘extra-protocol’ endeavours are completely *ad hoc*, receiving very little recognition. What is especially important about these *ad hoc* acts of care, however, is arguably not (only) treatment outcomes. Geissler et al (2008:704 original emphasis) and Whyte (1997) observe of MRC fieldworkers that, given few resources, their prime obligation was to “try to help”. It is these concerted efforts to “[make] an effort when faced with suffering” (Geissler et al 2008:705) that, like the mode of healthcare provision discussed previously, foster trust and build positive relations between TRO and the constituents of the Hareford region.

V. Cases of Abuse and Neglect

TRO’s follow-up teams also face a pressing challenge as a consequence of the conjunction of an impoverished material environment and the intimacies required by clinical research on TB: to look out for, and to report, cases of physical abuse and neglect. Implored by the doctrines of Good Clinical Practice (GCP), this requirement is cemented in law by the Children’s Act (2005), meaning that serious legal consequences could result from a failure to report such cases. Given the intimacies of the follow-up visits – accessing participants’ homes, physically examining them and, most importantly,

seeing them *naked* – the field teams are generally perceived as being in a position to notice when participants are being neglected or abused. Unlike the medical and contextual factors discussed above – which are often framed as opaque, esoteric, and necessitating a ‘trained’ biomedical perspective – the signs of neglect and physical abuse are framed as more transparent and ‘right there’ for the field researcher to see. As is to be expected, TRO take this issue very seriously. Speaking to Yvonne, she stated with conviction that abuse and neglect are, and should continue to be, an enduring concern of TRO as they continue their research in the Hareford region:

Now that you’re entering that environment ... I mean this is something that we’ve *always* thought about ... [It’s] impossible, actually, if you think about it, given what we know about our communities, not to know that kids are being abused, and what’s going on in these homes.

One would perhaps surmise that reporting cases of abuse constitutes an additional – if legally required – element of TRO’s ‘extra-protocol’ operations in the region. However, I became aware of a general perception among TRO’s research staff at the field office that while the follow-up teams encounter cases of abuse and neglect, they do not often report them, if at all. Yvonne stated:

But we’ve never heard anything back from our field workers that, you know, where they’ve found instances of abuse ... very seldom would something like that come up. We think they see it, they hear about it, but they sort of ignore it because it’s not part of their business, and they don’t want to get involved.

While I was out with Yolanda and Lucinda, I did in fact witness a high degree of sensitivity to the possibility of abuse and neglect in the homes of participants – asking, for instance, as to the cause of certain visible cuts or bruises. This eventually led me to question the dichotomy that had been forged in practice between the opacity of health-related signs and symptoms and the transparency of cases of abuse and neglect; more specifically, to the ambiguities inherent in the categories of ‘abuse’ and ‘neglect’ – and who exactly is to ‘blame’. Following Farmer’s (1996) work on “structural violence”, it is certainly difficult to determine any precise boundary between the ‘neglect’ of children by their parents and the inscription of an apartheid legacy into their skins. Moreover, even ‘abuse’ is more ambiguous than it might seem. Not only is ‘abuse’ arguably just as inseparable from the legacy of apartheid (with many young men feeling emasculated as a result of a lack of employment opportunities [Ashforth 2005]), but it is also often very difficult to determine the difference between a bruise caused by an abusive father and one caused because of a benign trip or fall. The distinctions are a complex entanglement of epistemology and political-economics.

More clear-cut cases of abuse and neglect are thought to exist. Rather than question the necessity of the Children’s Act (2005) or its effectiveness in ensuring the wellbeing of children in South Africa, however, in lieu of further research what I would like to do is briefly point towards the gaps, silences

and fragilities of trial communities that are easily overlooked. Geissler et al (2008:704-5) describe the ways in which the healthcare benefits afforded by participation in the MRC's MVT in The Gambia were distributed among community members. It was decided that free healthcare would be received by the 'families' of trial participants, where the definition of 'family' was defined according to affinal and biological ties (e.g. if a participant was unmarried, his/her parents would receive healthcare; but if married with children, their spouse and children would receive the benefits. It fell to the MRC fieldworkers, meanwhile, to mediate and attempt to dissolve the disputes that erupted when the ties and obligations generated on the ground between the MRC and the trial population transcended the predetermined "policy of exclusion" (2008:704). Similarly, while in theory the Children's Act is accorded categorical priority, the obligations generated on the ground make matters less straightforward. Without the cooperation of the families of TRO's participants, especially their mothers, an enduring clinical research programme of the sort run by TRO would not be possible. Not only do they 'consent' on their children's behalf to take part in the clinical trials, but they also allow TRO's researchers into their lives and livelihoods (even into their homes), let researchers to make physical contact with their children, take time out of work for the purposes of the follow-up visits and, if necessary, attend the CV ward for 48 hours. In the abstract, it is easy to conceptually separate 'participants' from their wider networks of sociality. But negotiating affective relationships on the ground, in areas that are sometimes dangerous⁸, the follow-up teams are in a difficult position, occupying a space of tension that is easily overlooked.

VI. Conclusion

In this chapter, I have explored the 'interface' of global medical research structures (as embodied by trial protocol) and local material realities, through 'following' protocol as it takes TRO's field teams into the Hareford region to conduct the follow-up visits. I demonstrated that the ground-level conduct of clinical research is permeated by a relational-affective dimension that is both necessitated by, though cannot be contained within, the requirements of protocol. The follow-up teams play a crucial and irreducible role in this regard, balancing a priori separations and emergent relations, and skirting the fine line between protocol and 'extra-protocol'. I therefore concur with Geissler and Molyneux (2008:688; see also Geissler et al 2008 and Gikonyo et al 2008) that the creative and dexterous role fieldworkers play at the 'interface' needs to be recognised as integral to the conduct of clinical research in resource-poor environments. But crucially, note the phenomena that I have highlighted in this chapter: the dexterity and relational knowledge required for finding participants and conducting the follow-up visits; the demands of balance 'less interpretation' with a 'holistic' gaze attune to context; the additional improvised and make-do practices of care; the requirement to maintain a

⁸ For instance, a stabbing occurred directly in front of one of TRO's vehicles, before the perpetrator help up the knife and threatened, "I know who you are and I'll get you next", to a shocked fieldworker. Aside from isolated incidents such as this, the recent strikes in the region are cause for concern.

critical eye for abuse and neglect on the naked bodies of infants. These complex relations and exchanges are inseparable from, firstly, TB as a socio-historical phenomenon in South Africa, where TB constitutes one among *many* challenges related to poverty. TB is not just a biological entity in this sense but fundamentally tied to a harsh material reality that characterises the post-apartheid Hareford region. Secondly, these relations and exchanges are enabled and shaped by the frequent and intimate requirements of trial protocol which are designed, paradoxically, with the aim of abstracting TB from context and relations in order to ‘objectively’ research it. Separations and relations, then, are two sides of the same coin, often in tension but mutually interdependent. Chapter 4 takes this discussion further in the more resourced medical setting of the CV ward, and the expertise, technologies and protocols that feature in it.

University of Cape Town

Chapter 4:

Separations and Relations in the CV Ward

I. Introduction

If reason is found during the follow-up visits that a participant might have TB, their mothers (or other close relative) are usually asked to bring them into the CV ward for 48 hours in order to determine whether they have TB disease. In what follows, through the narration of my experiences with TRO's researchers in the ward, like the previous chapter I explore the dynamics between separations and relations, protocol and 'extra-protocol' in and between the various tests and examinations that characterise the visits. After detailing the tightly controlled conditions in the ward and the particularities of protocol therein, I interrogate the two separate diagnostic processes for TB that TRO's participants are channelled through upon admission to the ward, and the ways in which they respond to the dual imperatives of ensuring both the production of 'objective' data and the wellbeing of participants. I then demonstrate that the CV ward visits are, like the follow-ups, taken as opportunities to provide healthcare that go beyond the requirement of the trial, and the mechanisms by which this is achieved. Finally, with particular reference to infants' weight in the process of diagnosing TB, I explore an instance of trial protocol running into tension with the commitment to the wellbeing of trial participants, and how the resulting tension is grappled with given temporal constraints and limited resources. I conclude that despite the tightly controlled conditions of the CV ward, its day-to-day operations, informed by the epistemological complexities of diagnosing childhood TB, are underwritten by material struggles, relationalities, and challenges that are an irreducible component of clinical research on the ground.

II. The Rhythms of the CV Ward

Early one morning, while I was still getting to grips with the rhythms of the CV ward, Monique – the ward's head nurse – invited me to watch the goings-on in the 'treatment room', situated down a hallway, and through a pair of swinging doors, from the main ward space. At the time, the participants who had been admitted to the ward the previous day were undergoing a procedure called 'sputum induction', the purpose of which is to procure a sputum sample that can be sent to TRO's laboratory in Cape Town and tested for TB (see Chapter 2 section IV). The room was cold, and permeated by the sound of various pieces of medical equipment hissing away, as well as the drone from a large

extractor fan attached to the ceiling. While Monique and Klara chatted amiably to one another, I watched with a mixture of fascination and trepidation as they went about performing the procedure on the infants. Firstly, with the aid of the infant's mother, a nebulizer mask was attached to the infant's face for precisely ten minutes, in order to 'loosen up' the contents of the infant's chest. Then, the nurses would wrap the infant in blankets in order to hold them securely down on the treatment table, before inserting a thin tube, attached to a suction device, up the infant's nose and down their oesophagus. As the suction took effect, sputum (and often a measure of blood) would fly up the tube and into a test tube, which was immediately sealed and placed in a container. The procedure was unpleasant to witness for someone who had not spent a great deal of time in biomedical settings before. But it was of course far more unpleasant for the infants, who usually cried throughout the proceedings, and for their mothers.

The sputum inductions are one of the more unpleasant aspects of a tightly scheduled series of tests and examinations that take place over a 48-hour period between admission and discharge⁹. During the day of admissions, the majority of the time is allotted to settling the participants and their mothers into the ward, which includes going through the CV ward's separate informed consent procedure, allotting them an open cubicle with a bed and a cot, and allowing them to meet with the other people who have been admitted that day. An array of toys are quickly scattered over the floor, and infants can be seen running around or flying through the ward on small bikes. Most of the subsequent socialising between adults takes place in a large communal kitchen area with a TV set. After they are settled in, the last requirements of the day are to weigh the infants again, perform a Mantoux skin test, an HIV test, and an X-Ray in the hospital's radiology department. Early the following morning, after a four hour 'starve' the infants visit the treatment room for the first time in order to have a 'gastric lavage' performed (this has the same aim as the sputum inductions but using a different method), before returning four hours later – and after another 'starve' in the intervening time – for the sputum inductions. Straight afterwards, to conclude the day's most unpleasant procedures, the nurses perform a quantiFERON blood test. Later in the day, the infants receive a physical examination by a clinical doctor, who, with the help of the infants' case files, both arrives at a clinical diagnosis of TB, and (if nothing is amiss) signs the CV ward discharge form. The next morning the infants are discharged, and their mothers will hear back in the following days from the field teams as to the results of the tests and examinations performed during the stay.

Once admitted to the ward, the entrances and exits of the CV ward are tightly policed (especially given that the ward is situated in a hospital inhabited by many TB-positive individuals), and, bar medical emergencies, it is rare for the study protocol to be interrupted. Whether the participants'

⁹ Blake (2007) importantly observes the analgesic effects that a mother's *touch* has in medical settings. While many of the requirements of the CV ward visits are unpleasant, the infants' mothers were in contact with them for most of the procedures, helping the nurses where possible. To my eye, this had a noticeable impact on the disposition of the infants during the 48 hours.

mothers arrive at the CV ward with the participants in the first instance is another matter. During the time I spent in the ward, it was very rare that all of the participants who were scheduled to arrive on a given date actually arrived – approximately two of every three, and on one occasion only three of a scheduled six. Monique and Klara cited a number of factors which prevent participants’ mothers from bringing their child to the ward: after two years in the study they were growing weary of its requirements; during the high season for wine farming it was particularly difficult to take time off work; and that the farmers, (mistakenly) suspecting that mothers received financial reward from TRO for attending the ward, were hesitant to allow them “paid leave”. Suffice it is to say that the contingencies of everyday life in the Hareford region are such that, in practice, visits to the CV ward in the interests of a bio-scientific experiment are not always feasible. Nonetheless, in spite of the often unpleasant tests and examinations and the difficulties of finding the required 48 hours, there are a number of medical benefits afforded by visits to the CV ward. Where the healthcare practices that punctuate the follow-up visits are characterised by long-distance surveillance techniques in the context of few resources, the CV ward is staffed by trained medical professionals, is more resourced, and is able to exploit the close proximity to the host hospital (cf. Samsky 2011:412). Therefore, in the following two sections I explore the dynamics between separations and relations, protocol and ‘extra-protocol’ in the context of face-to-face clinical interactions.

III. Clinical Diagnoses of TB

TRO’s participants are admitted to the CV ward primarily for the purposes of the clinical trial: through making diagnoses of TB, it can be determined whether or not the trial vaccine is efficacious in preventing the disease. However, given that TB is potentially life-threatening, TRO could not and would not simply send participants home were it to transpire that they are afflicted with the disease. They have to be *treated*. This entails either the referral of TB-positive participants to their local clinics (which are then responsible for the management of the infants’ treatment), or, in particularly serious cases, they are admitted to the host hospital’s children’s ward for a more prolonged series of treatments and therapies (this can last upwards of two years). If it is apparent upon admission to the CV ward that a participant is displaying severe symptoms of TB, then ensuring their immediate treatment is prioritised over completing the requirements of the trial. One participant’s lungs were in such bad condition when they arrived at the CV ward that, before trial protocol commenced, they were admitted straight to the hospital’s children’s ward.

The important task of determining that a participant is afflicted with TB and thus needs to be treated, however, is not entrusted to TRO’s diagnostic algorithm. The algorithm is designed to provide the most accurate diagnoses as possible within the constraints of using an impersonal, ‘one-size-fits-all’ diagnostic tool – which, as was discussed in Chapter 2, is the only way to render TB consistent with the ‘regulatory’ or ‘mechanical’ objectivity required for the purposes of data production (Kelly 2011; Simpson & Sariola 2012:565). The algorithm should not, for instance, be over- or under-

diagnosing TB, because this could lead the data to imply misleading conclusions about the efficacy of a vaccine. Thus, it is very particular regarding the signs and symptoms to which it lends significance: generally, with the exception of clinical manifestations, only when a sign or symptom is determinately indicative of TB is it taken into consideration when reaching a diagnosis. Meanwhile, the tests and examinations that constitute the various inputs to the algorithm are, as with the initial allocation of the trial vaccine, performed under stringent ‘blinding’ conditions. This is because the creation of an ‘impartial’ algorithm is insufficient to generate the sought after degree of ‘objectivity’ if the results for each participant are known to a researcher, whose judgements might be influenced accordingly. For instance, for every participant who is admitted to the CV ward, their chest X-Ray is read by three different interpreters, each of which knows nothing of the participants’ other test and examination results. At the end of the trial, the abstracted pieces of data from the tests and examinations are put together for each participant and streamed through the trial algorithm, which outputs a diagnosis that constitutes a trial endpoint.

However, it is precisely because of the desire to provide correct diagnoses *on aggregate* in the name of ‘objectivity’ that from time to time the varied and often subtle signs and symptoms by which the disease manifests will elude the algorithm. It is likely to ‘miss’ some cases of TB. Feerman (2011:173-4) notes a dramatic difference between what constitutes ‘evidence’ for doctors working in US American university hospitals and African government hospitals. Where the former’s evidence-base is informed by the imperative to contribute to academic research outputs, African doctors’ evidence-base is driven by the need to make immediate clinical decisions in the context of the “normal emergency” of healthcare provision in resource-poor settings. The CV ward is not under-resourced. However, the epistemological complexities of diagnosing TB in children are such that the ‘evidence’ acknowledged by the trial algorithm – which is aimed at research outputs – is not a sufficient *clinical* diagnostic tool alone, and needs to be supplemented with a more responsive evidence-base (akin to that of the African doctors referred to by Feerman [2011]). Thus it is that infants who are admitted to the CV ward are channelled through not one diagnostic process but two: one for the purposes of the clinical trial itself (via the trial algorithm), and one for exclusively clinical purposes. In the clinical context, because of the ease with which TB is ‘missed’, doctors consciously err towards *over*-diagnosing the disease. As Dr Janssen remarked during an interview, “as a clinician, if you're worried, rather put them on TB treatment, than miss it, and have them coming back with TB meningitis or something”. Part of this inclination towards over-diagnosis is that unlike the algorithm, which only accepts what are referred to as ‘hard’ signs and symptoms, is that in the clinical context diagnoses can be made on the basis of what are commonly referred to as ‘soft’ signs and symptoms. Such ‘soft’ indicators include: clinical manifestations of TB; a medical history which suggests TB (e.g. a failure to respond to antibiotics for more benign lung infections); and a ‘suspicious’ looking X-Ray (e.g. blotches which could be TB ‘glands’). Infants must still display a certain number of

accepted TB signs and symptoms before a positive clinical diagnosis of TB can be reached. However, within these constraints, a degree of discretion is afforded.

Importantly, the clinical diagnosis is performed not by an impartial tool but by a trained clinician who, visiting the CV ward during the second day of the 48-hour protocol (as was mentioned above), interacts with TRO's participants face-to-face. Occasionally, that doctor is one of TRO's, but more often, it is the host hospital's Dr Gilbert, who visits the CV ward in and between his rounds in the host hospital. Simpson and Sariola (2012:565-6) argue that Sri Lankan study doctors involved in RCTs felt that the 'blinding' procedures characteristic of the clinical trial were sidelining the trust and rapport that previously characterised the relationship between patient and doctor. This is surely the case. However, what I would add is that the 'blinding' procedures that give clinical trials their epistemic authority also sideline the relations *between* signs, symptoms and points of context that characterise the clinical gaze. Recall that in Chapter 3 it was observed that, in the shadow of the mechanical requirements of the follow-up visit 'form', the field teams are implored to maintain a 'holistic' purview that, while relevant to the trial to an extent, was largely used for 'extra-protocol' healthcare provision. Similarly (although with the benefit of face-to-face-interaction), unlike the isolated results that are fed into the algorithm, a crucial part of tenet of the clinical diagnosis of TB is that the results of each test and examination are known to the clinician. Indeed, part of being a skilled clinician is the ability to draw links between different and often subtle aspects of the human physiology. Often necessitating a girth of hands-on clinical experience, clinicians draw upon what Dr Janssen referred to as their "gut feeling" in order to see connections between signs and symptoms and ultimately to make diagnoses. Human (2011), for instance, narrates the diagnosis of patient Jonathon by a clinician, who, through observing "the rings around Jonathon's eyes", knew that he was suffering from TB. Speaking to Dr Gilbert, he explained to that he is quite happy, for instance, to be swayed by the knowledge that an infant in question has a positive Mantoux skin test when reading an X-Ray. Being able to draw links between various signs and symptoms is a central tenet of his diagnostic methodology, allowing him to determine the line between 'definitely not' TB and, if something is amiss or looks 'suspicious', to rather be 'safe than sorry'.

The significance of this is that while anthropologists of 'trial communities' (including myself in Chapter 3) have documented the important substantive relations and material transactions that take place in and between clinical trials – perhaps most importantly the 'extra-protocol' provision of healthcare – we can see here that these relations and transactions occupy a more central role. More specifically, the epistemological complexities of diagnosing childhood TB are such that un-blinded clinical practices – and the relationalities they entail – constitute an indispensable component of protocol itself (cf. Feerman 2011:173-4). The consequence of this is significant in the context of an impoverished environment in the Hareford region. Through the screening procedures that take place during the follow-up visits, the subsequent tests and examinations in the CV ward, and the clinical gaze that is brought to bear therein, TRO's participants are able to receive diagnosis and treatment,

perhaps earlier than might otherwise have been the case, for one of the most proliferate killers in South Africa today. This goes considerably against the grain of prevailing concepts as the ‘therapeutic misconception’¹⁰.

IV. Beyond Protocol in the CV Ward

TRO’s participants may be admitted to the CV ward primarily for the purposes of diagnosing – and possibly treating – TB. Nonetheless, as during the follow-up visits, ‘extra-protocol’ healthcare practices punctuate the tightly controlled experimental conditions in the CV ward. Monique explained to me that TRO’s participants often arrive at the CV ward with medical problems that are not – or not necessarily – related to TB. Study doctor Dr Hill said to me that even though these medical problems are not the concern of trial protocol, it is “very important”, as it is during the follow-up visits, that TRO ensure that participants receive the medical attention they need (a similar remark was made by Dr van Zyl in Chapter 3). This is the case even if the illness from which they are suffering means that they no longer meet the inclusion criteria for the trial and thus have to be excluded. As a result, when participants come into the CV ward, a part of her and the other nurses’ routine is handling these non-TB related medical problems (cf. Geissler et al 2008; Leach & Fairhead 2011; Kelly 2011). She even went so far as to say that she thought of her role in TRO’s clinical trials as being a “clinician first and a researcher second”.

Providing participants with healthcare for non-TB-related medical problems, however, has to be negotiated with the strict requirements of trial protocol, which makes the endeavour rather challenging. In the interests of creating the most ‘valid’ and ‘reliable’ clinical data as possible, the CV ward is treated to the best of TRO’s ability as a bio-scientific laboratory: its entrances and exits are tightly policed, variables within the ward are controlled, and, as was observed above, protocol is followed to the letter. The complexity this causes for the provision of ‘extra-protocol’ healthcare is that only certain medical conditions can be treated *within* the space of the CV ward, which is, according to study protocol, only supposed to house otherwise healthy babies that are showing signs of TB. Monique explained to me that, “my protocol and SOPs [standard operating procedures] state clearly it should be a healthy baby with TB signs”. In the event that a participant arrives at the CV ward and is showing symptoms of an illness or disease clearly *not* related to TB, what happens is that the nurses will refer the infant to Dr Gilbert, who treats the infant as if they had been referred to the host hospital from one of the clinics in the region. Depending on the severity, the illness may exclude them from the clinical trial. In instances where an infant develops a medical problem *after* having been admitted to the CV ward, for instance with diarrhoea or a high fever, protocol allows that the

¹⁰ The notion ‘therapeutic misconception’ arose during the 1980s in the context of concerns about the quality of informed consent procedures in clinical trials. It refers to the ‘mistaken’ view among participants that clinical trials are there to provide healthcare. Informed consent procedures therefore strive to dissolve this misconception in order that participants can make fully ‘informed’ and ‘autonomous’ decisions.

infants be treated in the hope that it will subside promptly. Therefore when the nurses observe a medical problem developing, they contact Dr Gilbert who, as a doctor, is in a position to prescribe drugs. If it appears that the condition is not going to subside, however, the participant will be referred to the host hospital for more comprehensive medical attention than is available in the CV ward.

Despite the complexities of providing and facilitating healthcare in the middle of a bio-scientific experiment, and that the more serious problems necessitate referral, the interventions made as a result of a visit to the CV ward are nonetheless important. Monique, commenting on the health-related benefits that participants receive from coming in to the ward, related to me one example:

One baby came in for failure to thrive. But when they [the nurses] did the physical exam, they could feel and see that around the abdomen there was some abnormality. They asked the study doctor to do an assessment, and she found that there was a blockage, and they referred to the special paediatric outpatients. This baby ended up at Tygerberg hospital with colon problems. So *ja*, it's good for the infants: a free x-ray, HIV-test, quantiFERON, and we look at the overall health of babies.

It must be stressed that these *would* in fact be 'free' through primary healthcare institutions in the region. What Monique was implying here is that actually *accessing* healthcare resources is not so straightforward, especially given the limited mobility of participants' mothers in the context of the day-to-day struggles of agricultural life (cf. Farmer 1996). The importance of TRO in the therapeutic landscape of the Hareford region is that, through both the follow-up visits and visits to the CV ward, it constitutes an effective point of access to these resources. This is the case not only for TRO's participants. While TRO generally perceive their responsibility as being exclusively to their 'participants' (i.e. the infants, as was particularly clear in Chapter 3 regarding cases of abuse and neglect), in the CV ward the nurses also pay attention to the wellbeing of participants' mothers. As Monique explained:

If a mum is coughing, you can see, we are all nurses, you can see someone's body language or facial expression when it's not well. So in informed consent, we'll ask if they're happy, you don't look satisfied, happy, are there any issues you'd like to discuss? They'll say, yes I'm worried about someone at home, I can't really stay for 2 days, or say I'm not feeling well, pain somewhere, I'm also coughing. So the nurse will ask Dr Gilbert or another doctor if we can do a chest x-ray, and they never refuse. The other night the night staff called to say it seems a mother might have breast cancer, a swollen painful breast ... So we let her call family to fetch her on the first evening ... She went to [another nearby] hospital. If they're coughing, or a skin rash, Dr Gilbert will also always try to prescribe something for them. That's the cool part.

I argued in Chapter 3 that one of the most important aspects of TRO's 'extra-protocol' healthcare initiatives during the follow-up visits is the *effort* that it demonstrates in the face of suffering, and the *relations* that are built in the process (Geissler et al 2008:705). That argument I would like to extend to the efforts that take place in the CV ward. While less of a 'presence' in the region than the movements of the follow-up teams in the TRO branded vehicles, it is an integral site at which the substantive relations and material transactions that constitute TRO's 'trial community' on the ground are established.

V. When Protocol Seems at Odds with Participants' Wellbeing

Although I have thus far demonstrated that the relationship between experimentation and healthcare provision during the CV ward visits are in many ways complementary, this is not without exception. As will have been clear from my descriptions of the tests and examinations for childhood TB, particularly the goings-on in the 'treatment room', the requirements of protocol are often very unpleasant for the infants. Monique noted that some of the participants, many of whom are almost two years of age, are old enough to remember the visits: "they're not babies anymore – they are old enough to remember, and they get affected". While there are of course health benefits as a result of these requirements, in particular the diagnosis and treatment of TB, Monique argued that some infants are admitted to the CV ward repeatedly when there is actually no need to do so – at least, insofar as the infants' wellbeing is concerned. Therefore, the requirements of protocol could be construed as somewhat at odds with participants' wellbeing.

One of the most significant clinical signs of TB, and thus one of the most common reasons for participants to be brought into the CV ward, is weight loss or insufficient weight gain ('failure to thrive'). This is the reason that TRO are as concerned as they are with keeping accurate track of participants' weight. However, Monique argued that the fact that some of TRO's participants were being repeatedly admitted to the CV ward on the basis of either weight loss or a 'failure to thrive', and found each time *not* to have TB (even by the more cautious clinical diagnostic process), is evidence that their weight problems are due to *other* factors. As I mentioned in Chapter 2, in the wake of the 'dop' system of payment in the region, the Hareford has high rates of alcoholism among farm workers, and, as a result, many infants are born suffering from foetal-alcohol syndrome. In such cases, infants are not going to be of normal weight "even if they live in the king's castle", as Monique put it. More commonly, however, the reason that infants are underweight or 'failing to thrive' is that they are under- or mal-nourished; that is, they are either not receiving enough sustenance, or not the right kinds of sustenance for normal weight gain. In chapter 3 I argued that, on the ground, TB constitutes one among many challenges related to poverty, and is thus intricately tied to a legacy of apartheid that left the constituents of the Hareford region in near-absolute poverty. Monique's observations beg a stronger argument. Given that there are a host of problems related to poverty that can cause weight loss or 'failure to thrive', of which TB is but one, TB is not only historically entangled with these

other challenges but *epistemologically inscrutable* from them – until further tests and examinations have been performed, that is. It is only *after* having been subjected to the 48 hour stays in the ward that the cause of the weight problems can be discerned.

Efforts have been made to prevent infants from being repeatedly admitted due to non-TB-related weight problems. It is beyond the scope of TRO's powers to do much about infants suffering from foetal-alcohol syndrome, except perhaps for remaining sensitive to it when deciding to admit afflicted infants to the ward. However, in instances where infants have weight problems due to their being under- or mal-nourished, there are feasible solutions. Firstly, as was discussed in Chapter 3, the follow-up teams are encouraged to remain vigilant for signs in participants' home environments that they are under- or mal-nourished, so that more informed decisions can be made regarding admissions to the CV ward. However, due to a lack of medical expertise this is not always successful. Secondly, and more significantly, participants with non-TB-related weight problems that pass through the CV ward – and determined as not having TB – are referred to the government feeding schemes, designed to provide infants living in impoverished households with a stable source of sustenance. The referral takes the form of a letter, composed by one of TRO's nurses, to the infants' local clinics, which are responsible for enrolling infants into the scheme and regularly distributing the required sustenance. This is in the interests of improving the weight of TRO's participants, and ultimately to prevent their being repeatedly admitted to the CV ward unnecessarily. But moreover (and barring the harms for which it is supposed to compensate), it arguably constitutes another aspect of TRO's 'extra-protocol' healthcare interventions in the Hareford region, facilitating the provision of sustenance where mothers might not otherwise ask for or know about it.

Whether TRO's participants actually *receive* the sustenance to improve their weight is another matter. There is a perception among some of TRO's on-site staff, for instance, that the food given for the infants is sometimes later sold on for the purposes of feeding alcohol addictions. A more common observation, meanwhile, is that when the mother of one of TRO's participants arrives at a local clinic with a letter from TRO referring the infant to the feeding scheme, the nurses do not always act upon it. When I was out with Yolanda and Lucinda, we visited a number of houses where it appeared that participants' mothers had presented the letter of referral, but had not been enrolled in the scheme. Yolanda remarked to me that:

The letter has [TRO]'s name all over it, saying that the infant is taking part in their study etc...But as soon as [the nurses] see it is [TRO] they go "meh" [dismissive expression].

The reasons for this I was unable to ascertain. But if true the implication is that, even though TRO's participants are referred to the feeding schemes in cases where they have non-TB-related weight problems, this is no guarantee that they will not be repeatedly admitted to the CV ward. It might be noted, however, that as with the follow-up teams' 'holistic' awareness, this was a measure only

implemented *after* the clinical trial have begun (in this case only a matter of months before my first research period with TRO). Whether successful or unsuccessful, for good or for ill, what this demonstrates is that challenges such as this cannot always be foreseen a priori, and it thus falls to clinical research organisations to continuously adapt their responsibility to participants in acts of what Mol (2008) calls “tinkering”. Such acts of tinkering cannot be ‘read’ out of trial protocols, nor easily foreseen at the abstract level at which discussions around medical ethics in developing world contexts are currently pitched.

VI. Conclusion

In the last chapter, I demonstrated the interrelationships and interdependencies of separations and relations, protocol and ‘extra-protocol’ in the context of unpredictability and dexterity, where theory struggled to translate into practice, and where available resources were largely outstripped by expectations. This chapter, by contrast, took place in the CV ward, a space of considerably more healthcare resources, greater availability of medical expertise, and more predictable and tightly-controlled conditions. What I have shown here, however, is that the epistemological complexities of diagnosing TB, and the intimacies that are necessitated thereby – a 48 hour stretch of uninterrupted medical contact, to be sure – are punctuated to just as greater extent as the follow-up visits by material adversities, and the relations and transactions that arise therewith. The diagnosis of TB, which constitutes the primary purpose of the CV ward visits, is torn between the dual imperatives of data collection (via the abstractions of trial algorithm) and the wellbeing of participants (via the relational gaze of the clinician), where the latter’s disposition towards over-diagnosis is implored by well-founded concern. The periods before, during and between TB diagnostic procedures present ‘extra-protocol’ opportunities to identify non-TB-related medical problems for both participants and their mothers. The relationships between TB, poverty and ‘weight’, meanwhile, present what is perhaps the clearest difficulty of abstracting TB from context: not only is TB historically inseparable but, prior to further tests and examinations, epistemologically inscrutable from a poverty-saturated legacy of apartheid governance. Attending the ‘interface’ in the CV ward – its separations and relations, protocol and ‘extra-protocol’ – the nurses and doctors that work therein play arguably just as under-acknowledged a role as fieldworkers, some elements of which arguably no amount of forward planning could have pre-empted.

Chapter 5: Conclusion

I. 'Trial Communities' in Resource-Poor Regions

The increasing expansion of clinical trials into resource-poor regions of the world has demanded ever more “immutably mobile” (Latour 1987) research structures, both in terms of formal ethical guidelines and the bio-scientific practices they govern. Integral to this mobility is that they are able to assume the form of a series of “ordered separations” that can be transplanted onto any given research locality without being significantly altered in turn. Thus the impetus on: predefined groups and entities, ‘blinding’ procedures, rigid protocols, adequate ‘communication’, and scrupulous documentation (Geissler et al 2008:700). Exploring clinical research at the ‘interface’ between global research structures and particular research localities, however, anthropologists of ‘trial communities’ have sought to unsettle the abstract and rather idealised imagining of the clinical trial (e.g. Geissler et al 2008; Gikonyo et al 2008; Geissler & Molyneux eds. 2011). Through the rigorous empirical study of the day-to-day conduct of clinical research in resource-poor regions, these anthropologists have importantly argued that the ‘ordered separations’ of formal ethics and bio-scientific methodologies are underwritten by a relational-affective dimension which is emergent, transactional, cognizant of material inequities – and often largely undocumented. Among the most significant elements of this implicit dimension are the “extra-scientific” (Geissler et al 2008:700) measures taken to ensure the provision of healthcare for participants, their families and communities; and the role that fieldworkers play on the ground negotiating the demands of research protocols, “extra-scientific” operations, and people’s fears, anxieties and concerns therewith (Fairhead, Leach & Small 2006; Leach & Fairhead 2011; Molyneux & Geissler 2008).

On the basis of ethnographic research at TRO’ field project office in the agricultural Hareford region of South Africa, I have explored the ‘trial community’ generated by its operations at the ‘interface’ of global research structures and the social dynamics of the region. The frequencies and intimacies – and consequentially *affective* character – of the interactions between TRO and the impoverished constituents of the Hareford region are such that, similar to the findings of other ethnographies, TRO’s researchers tread a fine line between separations and relations, protocol and ‘extra-protocol’. But what I have attempted to highlight in this dissertation is that these dynamics are shaped by TB as engaged and experienced at different levels of scale. In Chapter 2, I demonstrated that TRO’s trial community has been brought together by a global imperative to produce a booster vaccine for the current BCG (cf. King 2002), one which has enabled the conduct of

over eleven clinical trials in the Hareford region and, as a result, an enduring relationship with the region's constituents. I then observed that the epistemological complexities of diagnosing childhood TB, and how they have been grappled with, have resulted in a trial protocol characterised, paradoxically, by a particularly frequent and intimate pattern of interactions between researchers and participants. Therefore, while I had not yet explored the substantive 'glue' in which trial communities consist – or even described protocol in too great a detail – what I demonstrated was how and why TRO's 'trial community' has the particular 'shape' it does, against which life at the 'interface' can be seen to unfold.

II. Life at the 'Interface': the Follow-Up Visits and CV Ward

Chapters 2 and 3 were situated at the 'interface' localities of the follow-up visits and the CV ward, where TRO's clinical trial carries TRO's research staff into the most direct routine contact with the constituents of the Hareford region and the impoverished circumstances in which they live. The preoccupation of these chapters was demonstrating that 'objective' research into TB vaccines – through a particularly shaped trial protocol – has generated a relational-affective dimension that is necessitated by, though cannot be contained within, its written demands. Through describing protocol in greater detail and then 'following' it through the ward and the field, I traced the fine line between separations and relations, protocol and 'extra-protocol'.

The follow-up visits would simply not be possible, for instance, without the dexterity and relational knowledge possessed by the field teams, who on a day-to-day basis navigate both space and people in order to 'screen' for TB (as per the prescribed 'form'). The researchers in the CV ward are not so burdened, instead occupying a space where participants and their mothers – more often than not – travel to them for extensive tests and examinations. Yet in the CV ward as in the follow-up visits, 'ordered separations' are met and exceeded by relations and affectivity. Of particular note is the ways in which a 'clinical gaze' – attune to context, links, and subjectivity – features in day-to-day life during the follow-up visits and in the CV ward. Somewhat at odds with the more formal requirement for 'less interpretation' during TB screening procedures, in the context of the follow-up visits it shows up at the fringes in the interests of ensuring 'extra-protocol' healthcare provision. A similar story is true of the CV ward, where the maintenance of a critical eye for medical problems can also lead to positive 'extra-protocol' treatment outcomes. But particularly noteworthy is the indispensability of face-to-face clinical practices in the process(es) of diagnosis, where the epistemological complexities of diagnosing childhood TB are such that an integral component of protocol is the levelling of a clinical gaze on the bodies of participants. Where TRO's 'extra-protocol' operations could be construed as somewhat peripheral, not a 'part' of the study – although I would strongly disagree – it is more challenging to make that case of TRO's engagements of TB. As far as participants' mothers are concerned, the 'real' endpoint of the trial might be that their child receives diagnosis and possible

treatment for one of the most proliferate and deadly diseases of poverty in the Hareford region. Supposed ‘therapeutic misconceptions’ aside, would they be wrong?

The ‘interface’ is not only a locus of potential healthcare benefits unacknowledged by formal medical ethics and prevailing bio-scientific knowledge practices, but also of a number of significant challenges. The desire on the part of TRO’s study doctors to use the follow-up teams to screen for additional medical problems is, while often successful, hampered by the dissonance between expectations and available resources. The Children’s Act (2005), while attuned to the South African context, is not so straightforward to implement in practice, wherein the follow-up teams have to negotiate affective relations developed within participants’ wider networks of sociality. Meanwhile in the CV ward, the potentially beneficial outcomes of the 48-hour stays are unsettled by the possibility that participants are sometimes unnecessarily subjected to the often unpleasant requirements of protocol. Underlying this challenge is the fact that the symptoms of TB and of an impoverished environment are *prima facie* indistinguishable. While a number of feasible solutions have been implemented, including the referral of children with non-TB-related weight problems to the government feeding scheme, this is a challenge not easily resolved. Nonetheless, these challenges, and the balancing acts from which they result – between separations and relations, protocol and ‘extra-protocol’ – are intricately tied to TB as it transcends levels of scale: the global public health imperatives driving an enduring clinical research programme in the Hareford region; the development of trial protocol in a complex epistemological setting; and on the ground as inseparably tied – both historically and epistemologically – to a legacy of apartheid governance. *It is in the space of interdependencies, contradictions and tensions between levels that the substantive relations and material transactions in which TRO’s ‘trial community’ consists unfold.*

III. Evidence, Ethics and Emergence

Anthropologists of ‘trial communities’ for the most part do not desire that the “ordered separations” of formal medical ethics and the bio-scientific knowledge practices they govern be either removed or replaced in light of their findings. Geissler and Molyneux (2008:687) wisely argue that formal medical ethics and the neoliberal, rights-based vocabulary that holds currency therein have an important part to play in ensuring that clinical research organisations can be held accountable for their operations in resource-poor regions. Similarly, Kelly (2011:233-4) notes the democratic origins of ‘blinding’ and ‘randomisation’ in redistributing both epistemic authority and scarce medicines from an elite few to a wider public. What is deeply troubling however is that the emergent relational-affective dimension of clinical research on the ground is being systematically obscured; in formal ethics because of a suspicion of transactions in unequal encounters (Geissler et al 2008:700; Fairhead, Leach & Small 2006; Leach & Fairhead 2011); and in bio-scientific discourse because of concerns with ‘bias’, ‘subjectivity’ and their cognates (Kelly 2011; Simpson & Sariola 2012). These anthropologists therefore urge that of the more emergent aspects of clinical research at the ‘interface’

– relations, transactions, contingencies, challenges – be accorded more formal recognition in both formal ethics and scientific discourse; as should the crucial, creative, and ethically charged role that researchers, particularly fieldworkers, play therein (Geissler et al 2008; Gikonyo et al 2008; Leach & Fairhead 2011; Molyneux & Geissler 2008:688).

On the basis of my research with TRO’s researchers in the Hareford region, I could not agree more. What I have offered in this dissertation, however, is one thread – of which I am sure there are many – through which to explore the emergent elements of clinical research, and the ways in which those generated in one location contrast with those of the next. That is: the particularities of diseases ‘under the microscope’, in both their social and biological capacities, as they transgress multiple levels of scale; from their appearances in global public health discourse, through their implementation in research protocols, to their more concrete manifestations in particular research localities. In the context of the increasing penetration of medical research programmes into resource-poor regions of the world, threads such as this might prove useful analytical and methodological tools for anthropologists interested in further probing their and effects and possibilities. While different threads may have their own explanatory potentials, by way of a closing observation this particular one offers an interesting angle through which to acknowledge the efficacy of – and confer a certain epistemic authority upon – clinical researchers at the ‘interface’. Fuelled by the imperative for transportable and comparable clinical data, TRO’s research targets ‘TB disease’ as an abstract, individual, and transportable clinical category. However, what TRO are confronted with first and foremost is a phenomenon which is not abstract, individual, or transportable. TB on the ground, in its lived qualities, is inseparable from a legacy of apartheid governance and the multifarious diseases and challenges that have ensued. It is those who grapple with *this* TB that perform the productive, transformative and ethical labour required to extract ‘TB’ from context – to render it ‘global’. In this respect, TRO’s researchers, and others who, like them, are engaged in clinical research at the ‘interface’, are not mere “placeholders” of immutable research structures (Latour 2005; see also Simpson & Sariola 2012:557). They are, to the contrary, the frontline agents of an underlying and indispensable clinical metaphysics.

IV. Postscript

In the intervening time since the bulk of this dissertation was written, the results of TRO’s early efficacy clinical trial have been published. It was found that the prospective booster vaccine provides no significant protection against pulmonary TB in infants. But while this clinical trial may be a failure in some respects – though some have praised it for its operational success – TRO is already engaged in more TB vaccine clinical trials with the constituents of the Hareford region. The ‘trial community’ – which is, as I pointed out earlier, greater than the sum of its individual clinical trials – has endured. TRO may exist for the ‘greater good’ of future vaccines; but its more immediate contributions are arguably just as important.

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