

EXPERIMENTAL VALUES

Indian Clinical Trials and Surplus Health

TWO PROMINENT INDIAN physicians recently described the clinical trials of new drugs in India as a ‘new colonialism’. In an article published by a leading US medical journal, Samiran Nundy and Chandra Gulhati drew particular attention to ‘illegal and unethical trials’ conducted without regulatory approval.¹ But a moral critique of this kind, however legitimate in its own terms, does not adequately grasp the network of economic and social relations that the international health industry has established on a global scale. Even if all clinical trials conducted in India or other Third World countries adhered to the letter of the law and the spirit of ethical codes, the very structure of this network would remain one of exploitation. I shall outline here the dynamics of clinical trials in India, focusing especially on the huge capacity currently being built up in anticipation of the transfer of global trials to the subcontinent. This will provide a basis for interpreting the phenomenon in terms of concepts developed by myself and others currently researching this field, particularly those of *biocapital* and *surplus health*.

I. THE LANDSCAPE OF CLINICAL TRIALS

Clinical trials are the set of practices required to certify a new drug molecule as safe and efficacious for the market.² In the United States, the clinical-trials procedure is an elaborate one, conducted in a number of stages and contributing to the immense time, risk and expense of the drug development process. First, there is pre-clinical toxicological testing of a potential new drug molecule. This is usually performed on animals,

in order to determine whether the molecule being tested is safe enough to put into a living system. The second stage is that of dosage studies, designed to come up with a metric for the dose of the drug to be administered. Predictably, the efficacy of a drug increases with its dose, but so too does its toxicity; the aim is therefore to find an optimum range within which efficacy is maximized without too greatly compromising safety. If the drug is too toxic when tried on animals, the trial will not proceed any further, but if acceptable dose ranges can be determined, the third stage is a three-phase trial in humans. Phase 1 trials are conducted on a small number of healthy volunteers to test the drug's basic safety, since drugs that seem safe in animals may still show adverse effects in humans. Phase 2, which serves as a bridge, involves larger, scaled-up efficacy and safety trials on as many as a few hundred subjects, who may be either patients or healthy individuals. Phase 3 involves large-scale randomized trials on several thousand people, usually patients suffering from the ailment for which the therapy has been developed. These trials are frequently co-ordinated across multiple centres, increasingly on a global scale.

The sponsors for trials are generally biotechnology or pharmaceutical companies, since drug development in the US and most other parts of the world is undertaken largely by the private sector. Universities and publicly funded laboratories play a major role in the early stages of discovery—the identification of potential lead molecules and the conduct of pre-clinical tests—but the institutional structure of drug development is such that they increasingly license promising molecules to corporations that take them through clinical trials. This means that the biomedical and experimental rationales for clinical trials are completely

¹ Samiran Nundy and Chandra Gulhati, 'A New Colonialism?—Conducting Clinical Trials in India', *New England Journal of Medicine*, vol. 352, no. 16 (2005), pp. 1633–6.

² Clinical trials have become a site of keen interest in the anthropology of science. See especially Melinda Cooper, Brian Salter and Amanda Dickinson, 'China and the Global Stem Cell Bioeconomy: An Emerging Political Strategy?', *Regenerative Medicine*, vol. 1, no. 5 (2006); Joseph Dumit, *Drugs for Life*, Durham, NC forthcoming; Jill Fisher, 'Human Subjects in Medical Experiments', in Sal Restivo, ed., *Science, Technology and Society*, Oxford 2005; Wen-Hua Kuo, 'Japan and Taiwan in the Wake of Bio-Globalization: Drugs, Race and Standards', PhD dissertation, MIT 2005; Adriana Petryna, 'Ethical Variability: Drug Development and Globalizing Clinical Trials', *American Ethnologist*, vol. 32, no. 2 (2005), pp. 183–97; and Petryna, 'Drug Development and the Ethics of the Globalized Clinical Trial', Princeton Institute for Advanced Study Occasional Paper 22 (Oct 2005).

entwined with the market value these companies see in the drugs that eventually get developed, and the market risk that attends the drug development process. According to the Healthcare Financial Management Association's newsletter, 'twenty years ago, 80 per cent of clinical research trials were conducted through academic medical centres. In 1998, estimates indicated the number of [these] centres as investigator sites had dropped to less than half.'³ Health research and production is thus progressively captured by capital, and now needs to be seen as a semi-autonomous branch of it.⁴ The organizational complexity of clinical trials does however mean that it has been hard for pharmaceutical companies to manage them, leading to the emergence of an entirely new sector devoted to the management and administration of clinical trials. These companies, known as clinical research organizations (CROs), are now an integral part of the overall biomedical economy.

A plurality of actors

The movement of clinical trials to international—non-US—locations started in earnest in the mid-1990s. Adriana Petryna cites figures that point to a dramatic growth in the number of human subjects recruited into these trials, from 4,000 in 1995 to 400,000 in 1999.⁵ A recent study by the consulting firm A. T. Kearney shows that roughly half of the 1,200 US clinical trials in 2005 made use of an international site.⁶ In the 1990s, as Petryna notes, most of this growth occurred in countries that had agreed to harmonize standards in commercial drug testing with the guidelines set by the International Conference on Harmonization of

³ Indeed, law and policy scholars Tracy Lewis, Jerome Reichman and Anthony So have argued for public funding of clinical trials as a crucial mechanism to make essential therapeutics more accessible—and therefore to move health away from being an abstract market value towards being about healthiness. See Tracy Lewis, Jerome Reichman and Anthony So, 'The Case for Public Funding and Public Oversight of Clinical Trials', *The Economists' Voice*, vol. 4, no. 1 (2007). For the Healthcare Financial Management Association's figures, see Jennifer Jones and Alan Zuckerman, 'Clinical Research Trials: Creating Competitive and Financial Advantages', *Managing the Margin Newsletter*, available at www.hfma.org.

⁴ This is an example of what Etienne Balibar has described as the continual expansion of the value form and the infinite process of accumulation. Etienne Balibar and Immanuel Wallerstein, *Race, Nation, Class: Ambiguous Identities*, London and New York 1992, p. 180.

⁵ Petryna, 'Drug Development'.

⁶ A. T. Kearney Report, 'Make Your Move: Taking Clinical Trials to the Best Location', 2006; available at www.atkearney.com.

Technical Requirements for Registration of Pharmaceuticals for Human Use. These primarily included Latin American and Eastern European countries, but not yet India. Over the past two years, however, India has become one of the most dynamic sites for the establishment and growth of clinical research.

In India, a range of local actors currently see the country as providing an extremely attractive destination for outsourced clinical trials from the West. Contract research in the Indian pharmaceutical industry is already robust, and was estimated by the Chemical Pharmaceutical Generic Association to be worth between \$100 and \$120 million in 2005, while growing at 20 to 25 per cent per year.⁷ A further influx of global clinical trials is eagerly awaited. Who are these actors, and upon what do they base their expectations?

The most central, perhaps, are members of the burgeoning CRO industry. These are the most immediate beneficiaries of trials coming to India, and are therefore keen to create conditions for these trials to grow in a sustained and streamlined fashion. CROs are the major drivers of the build-up of clinical-research infrastructure, and particularly influential in building a regulatory framework for the conduct of trials. It is estimated that there are approximately a hundred CROs of reasonable size operating in the country at the moment. Some of these are fairly well established, with a couple being fifteen to twenty years old. A number of the better-known CROs were seeded in the late 1990s; many, however, have emerged only in the very recent past.

The Indian pharmaceutical industry is another interested party. It is in the process of retooling its business model in the wake of India's signing of the patent regime imposed by the WTO. Indian patent laws formerly allowed only process and not product patents on therapeutic molecules. This meant that one could not patent a drug itself, only the specific manufacturing process that produced it—allowing Indian pharmaceutical companies to reverse-engineer generic versions of drugs that had product patent protection in the West. The WTO regime now rules out such reverse engineering for the twenty-year duration of

⁷ As cited by the Indian Brand Equity Federation, available at www.ibef.org. These figures include contract work that is generated domestically as well as by foreign sponsors—not just clinical-trial activity, but also the manufacturing of active pharmaceutical ingredients.

the patent. This has forced a number of leading Indian drug companies into an R&D-driven business model, whereby they, like their Western counterparts, engage in the much riskier process of new drug discovery and development. Clinical trials become a constitutive part of this business model, because new drugs cannot be developed without subjecting them to an elaborate regime of safety and efficacy testing. In other words, the Indian pharmaceutical industry has itself served as a spur to the CRO sector. WTO entry may also have made India a more attractive research destination from the perspective of Western trial sponsors seeking to outsource, since their intellectual property is better protected under such a regime.

A third set of actors consists of the regulatory agents of the state. The immediately responsible body in India is the Drug Controller-General of India, roughly equivalent to the US Food and Drug Administration. This body, a fairly peripheral presence on the Indian regulatory landscape until a few years ago, is now in the process of recreating itself as a serious agenda-setting organization. The Ministry of Science and Technology is also actively involved through its Department of Biotechnology, which sees clinical research as part of a wider initiative to make India a global biotechnology power. It has pumped money into biotechnology and clinical-research initiatives, especially to open institutes that can perform or facilitate such research around the country. The Department is currently funding several new clinical research training centres around India, and has invested the equivalent of \$1 million in this field.⁸ Building the human-resource capability to conduct and monitor trials in India is a key challenge, and a number of entrepreneurial ventures are fully engaged in training the labour force required. Finally, there are the physicians who actually conduct the trials, though in the Indian context they have a relatively marginal presence compared to the CROs in setting the infrastructural and regulatory agenda for research.

There is a strong common interest among these actors—though this applies somewhat less to physicians—not just in building up a research

⁸ According to a speech given by M. K. Bhan, director of the Department of Biotechnology, inaugurating the BioAsia 2006 conference in Hyderabad, 9 February 2006. The day before, the Department's budget had been increased by 25 per cent, indicating both the serious prioritization of biotech by the Indian government and that lack of resources is no longer the issue when it comes to certain types of science and technology in India.

infrastructure in India, but also in promoting the country as a global destination for clinical trials. The experimental potential of Indian populations as trial subjects melds seamlessly with the market potential that Indian CROs perceive from an influx of these trials, and this convergence is facilitated by a larger historical moment that sees the Indian state branding and marketing itself to investors at global forums.

Economics and ethics

Some of the enthusiasm around clinical trials within India is mirrored in the West by agents who might outsource clinical trials to the country. For the most part, however, the anticipated surge in trial contracts to India remains speculative. The infrastructure-building occurring in India is very real; but it is a bet on future outcomes that, like any other speculation, may or may not pay off. To understand the clinical-trial situation in India, we must consider both the enthusiasms and the reservations of Western agents.

The anticipation of global clinical trials coming to India is based on the expectation that it would serve the interests of Western trial sponsors—especially US biotech and pharmaceutical companies—to outsource these trials to the subcontinent. This is at one level a general market expectation; a 2002 McKinsey report, for instance, estimated that clinical research in India will be a \$1 billion industry by 2010.⁹ Estimates of this kind have their own repercussions, triggering certain actions on the part of agents both in India and in the West.

The various perceived advantages in taking clinical trials to India include, among others, that of cost; estimates suggest that overall clinical-trial expenses for a multinational company could be reduced by 30 to 50 per cent, thanks to lower labour and infrastructure costs. There is also a perceived recruitment advantage—the assumption being that it is easier to obtain Indians for such trials, especially ‘treatment-naïve’ subjects. A major problem for drug companies conducting trials in the US is that Americans are therapeutically saturated, already taking so many drugs that it is hard to determine the efficacy of the molecule being tested without having to confront a whole range of interactions that muddy the data considerably.

⁹ NASSCOM—*McKinsey Report*, 2002; available at www.nasscom.in.

Other factors come into play when assessing the attractiveness of a country as a clinical-trial location. The recent report by A. T. Kearney, which provided an ‘attractiveness index’ for countries as trial destinations, considered—in addition to cost efficiency and patient pool—‘regulatory conditions’, ‘relevant expertise’ and ‘infrastructure and environment’. Indian actors are focusing on these three key areas as part of their capacity-building efforts; and indeed, Kearney already ranks India as the second most attractive destination, after China, for clinical trials outside the US. India scored much higher than the US in terms of patient pool and cost efficiency, but lower on the other three counts.¹⁰

However, the scenario is more complicated than one in which Western multinationals are tearing down the door to exploit cheap Indian populations. For early-stage trials in particular, it is uncertain how strong the pressure is for Western companies to outsource to India. There are obvious advantages in terms of cost and the ease of volunteer recruitment; but there is also a downside in terms of the relative difficulty of monitoring trials—very important if the data generated is to pass muster with the FDA—and the potential public-relations disaster that could attend an early-stage trial that went disastrously wrong in a Third World context. Indeed, the Kearney report points out that in August 2005, the top twelve pharmaceutical companies were running 175 ongoing trials in Germany—attractiveness index 4.69—and 161 in the UK—attractiveness index 5.0—compared to 26 in India, which had an attractiveness index of 5.58. In 2004, Pfizer invested roughly \$13 million in clinical trials in India, but this is put in perspective by the fact that its total global R&D expenditure was \$8 billion. Perhaps more than pharmaceutical companies themselves, it is Western CROs who see real value in finding new destinations for some of their already outsourced activity. Therefore, while there are convincing market rationales for taking trials to India, and an already strong flow of trials there through the multinational CRO industry, much of the capacity building in clinical research in India is still a bet on potential value from trials that could be outsourced in future.

Capacity building in this context means something far more extensive than the experimental infrastructure for conducting clinical trials, which is perhaps the easiest component in a country like India where material

¹⁰ A. T. Kearney Report, ‘Make Your Move’.

and financial resources are no longer so limited. This most basic aspect of capacity building also generates the least concern among Indian actors trying to attract trials into the country. A more elaborate challenge is building an adequate regulatory infrastructure, which needs to be far stronger if India is to host global trials.¹¹ This is especially so for trials outsourced from a US-based sponsor, which needs to meet the FDA's stringent criteria. Adriana Petryna has argued for a state of 'ethical variability', suggesting that ethical practices for clinical trials vary between First and Third World locales.¹² While in practice it is quite possible that the implementation of ethical guidelines is ultimately stricter in the First World, it is important to note the very serious attention now given to ethics by both the Indian regulatory agencies and the CRO industry there. Of equal importance is what such ethics comprise, and what is left out.

An ethical-trial protocol is primarily concerned with the question of informed consent. This includes the entire apparatus surrounding the consent process, especially an institutional review board infrastructure. Ethical practices in India are enshrined in guidelines that the government published in 2001. In 2005, these guidelines were converted into laws, known as Schedule Y. Interestingly, India is the only country in the world where the violation of good clinical practice is a criminal rather than a civil offence. At the same time, global trials that are valid in the eyes of the FDA need to be harmonized with what are known as International Conference on Harmonization protocols. Indian regulators are thus currently involved in a massive standardization process, driven by the Indian CRO industry. As legally embodied, then, Indian ethical guidelines are likely to be at least as stringent as those for the conduct of clinical research in the US, and in some ways more so.

Members of India's CRO industry bristle at the suggestion that clinical trials will move to India because it is possible to cut ethical corners there. This idea has been part of the debate around Indian clinical trials, and acquired salience and legitimacy because of the article by Nundy and Gulhati cited above. CRO leaders are acutely aware of the need to build a positive media image for their industry, and place great emphasis on the ways in which Schedule Y exceeds the demands of the International Conference on Harmonization. Specifically, Schedule Y is concerned

¹¹ Also essential to capacity building is the establishment of human-resource infrastructure, likewise the infrastructure for managing data generated by the trials.

¹² Petryna, 'Ethical Variability', 'Drug Development'.

with ensuring extra care in gathering informed consent from illiterate subjects and in considering what might constitute ‘ethical’ compensation for poor subjects recruited into early-stage trials—the logic here being that lucrative remuneration can actually act as a coercive incentive. One Mumbai-based CRO executive, Arun Bhatt, was typically emphatic about the importance of Schedule Y and good clinical practice: ‘We are new. We don’t want to play with the evolution of ethics.’¹³

Outside the enforcement potential of Schedule Y, however, a larger regulatory body with the scope of the FDA is still absent. As mentioned earlier, the Drug Controller-General of India is the nominal equivalent, but its remit is still basically limited to approving drugs for the market or for import into the country. Part of the regulatory effort currently under way in India consists in building a more substantial regulatory body with oversight powers that parallel those of the FDA, and whose conduct can be harmonized with that of its US counterpart. This was a central recommendation of the Mashelkar Committee Report of October 2005, which proposed a National Biotechnology Regulatory Authority that would regulate not just pharmaceuticals, but also agricultural products, transgenic crops, food and feed, and transgenic animals and aquaculture.¹⁴

Ethics, legally enshrined and contractually enforced, are integral to the capacity-building effort around clinical research in India. Members of the CRO industry are the most active drivers in building an ethical regulatory infrastructure. Nonetheless, the form this ethic takes—quite literally, the ‘informed consent’ form that the volunteers sign—does not mitigate the fundamental structural violence of clinical trials conducted in the Third World. I will elaborate on this below, developing a critique of the movement of clinical trials to India in the context of the global logics of biocapital and surplus health. The clinical-research landscape in India cannot be reduced to the neo-colonial exploitation of the local population as ‘guinea pigs’ by rapacious multinational interests, where

¹³ Interview with the author, 24 February 2006.

¹⁴ Ramesh Mashelkar, the head of the committee that wrote this report, was from 1995 until his retirement in 2006 Director-General of India’s Council for Scientific and Industrial Research (CSIR). He has been one of India’s most influential science policy-makers since independence, responsible in large measure for the aggressive embrace of global market values by the country’s scientific establishment. For a longer account of Mashelkar and CSIR, see my *Biocapital: The Constitution of Postgenomic Life*, Durham, NC 2006, especially Chapter 5. The Mashelkar Report can be viewed at www.biospectrumindia.com.

cutting corners is the norm and ethics easily sacrificed. A more nuanced analysis would take account of the desire on the part of the Indian state and corporate actors for the country to become a global experimental site, while noting that a comprehensive attention to ethics is quite compatible with the structural violence of global biocapital.

2. 'GOOD CLINICAL PRACTICE': A CASE STUDY

The concern displayed by Indian actors, especially the CRO industry, with what is referred to as good clinical practice is primarily focused on the proper protocols for obtaining informed consent at the time of trial enrolment, and with adequate monitoring of the clinical trials. In order to advance towards a critique of biocapital and surplus health, it is necessary to demonstrate the limitations of ethical practice in the Indian context and, by extension, elsewhere in the Third World.

Consider, for instance, the case of Vimta Laboratories, based in Hyderabad. Vimta can claim in many ways to be the gold-standard Indian CRO. Founded in 1991, it is one of India's oldest; it is the only CRO that is publicly traded on the Bombay Stock Exchange, and the only one in the country that has been audited twice by the FDA—passing both times with flying colours. The clinical-research manager of a US company whom I talked to suggested that Vimta was exactly the sort of Indian CRO with which she would consider collaborating.

Vimta's concern with informed consent, and its processes for securing it, exemplify the insistence on good clinical practice in India. On a visit to Vimta as part of my fieldwork, the first room I was shown was the waiting and screening room. This looks like the waiting room of a railway station; subjects come in and are given their consent forms, along with a basic questionnaire to determine whether they are qualified to participate, in this case in a Phase 1 trial. The walls of the waiting room are empty, except for a single bulletin board. This outlines all the risks that could accrue to participants in a clinical trial, but it is written only in English. I was told that in order to participate, subjects have to be literate—though not necessarily in English—and male; Vimta only enrolls females if the trial sponsor specifies a need for female subjects.

Beyond the waiting room is a long corridor, off which are a number of rooms where different types of medical examination are conducted on trial volunteers. First, their height and weight are recorded. If the subject weighs less than 55 kilos he is not accepted, as the risk of complications is too high. There is then a general physical exam, after which the tests become progressively more invasive; an ECG is conducted in a third room, blood drawn in a fourth—and sent to the pathology lab for analysis—and an X-ray taken in a fifth. I learned while being walked through this corridor that the consent forms the subjects sign in the waiting room are only for the medical screening procedures—if they are selected to participate in the trial, they sign a separate form, specific to the trial in which they are enrolled.

A number of the trials conducted at Vimta are Phase I trials on healthy volunteers. Recruiting subjects for these trials, as I mentioned earlier, has become increasingly difficult in the United States. I was told that volunteer retention is much better in India than in the US, because ‘people trust doctors here’. Interestingly, while it is in principle a challenge to recruit healthy people to have risky molecules administered to them, the entire set-up here seems to emphasize ‘selection’—almost as if being accepted for a trial were a test that only those who are fit enough can pass. Moreover, the subjects are only ever referred to as ‘volunteers’, suggesting no doubt their autonomous rational agency, the same agency that is contractually codified through the consent form.

No access to drugs

Such deep and, I believe, sincere concern with informed consent and good clinical practice, reflected both in national laws and in the practices of companies such as Vimta, does not, however, even touch on the major question of access to drugs. In the US, clinical trials at least implicitly suggest a social contract in which a small number of people are put on potentially risky medication for the sake of a larger social good—the development of new therapies. Those recruited into Phase I trials tend to be less well-off in the US as well, so that the social contract can never be a pure liberal one between rational individuals in what John Rawls would call an ‘original position’ of assumed equality.¹⁵ Nonetheless, there is an animating liberal sentiment which absolutely presumes that

¹⁵ John Rawls, *A Theory of Justice* [1971], Cambridge MA 1999.

the therapy, if developed, will eventually be accessible. And even if this is access via the market, for a price, thus raising issues of affordability and distributive justice, these issues can in principle be addressed through liberal welfare-state mechanisms. In the Indian context, by contrast, there is no guarantee that an experimental drug tested on a local population will necessarily be marketed there after approval—let alone be made available at an affordable cost. The Indian state has made no moves to ensure this, for example through such mechanisms as compulsory licensing regulations. The likely outcome is therefore a situation where Indian populations are used purely as experimental subjects, without the implicit social contract of eventual therapeutic access.¹⁶

The question of access to drugs is certainly a live one in the Indian medical community, leading to critiques such as that of Nundy and Gulhati. A leading Delhi-based psychiatrist in a prominent private hospital—who preferred to remain anonymous—told me that ‘while we understand the need for conducting trials, there is need for more uniform regulatory control’.¹⁷ This is not someone outside the circuit of clinical research; he is himself engaged in testing a number of psychiatric drugs. Most of the trials such prominent physicians conduct, however, are categorized as Phase 3, and involve patients they are treating, which puts their practice under a different ethical calculus—having to do with pastoral care—from that of CROs looking to increase Phase 1 trials on healthy volunteers, where the issue is simply one of experimental subjectivity. The relationship of such trials to drug access is an acute question for this physician, especially as regards subjects who may need to continue taking the experimental medication that is tested upon them if it is shown to have positive effects. The only mechanisms that exist to provide such access, however, arise from the policies of the companies sponsoring the trials, or the concerns of the centre conducting the trial. The same physician told me: ‘In the last two trials, the companies said they’ll try and make the drugs available. We have yet to see if that will happen. If it doesn’t happen, then we will only participate with companies that give an absolute commitment.’

While this physician and the hospitals where he works might be willing to take such an uncompromising stand on linking clinical

¹⁶ In contrast, Kristin Peterson has found in her research in Nigeria that the dominant issue is access to drugs. Meanwhile, the ethical/regulatory infrastructure is far from robust.

¹⁷ Interview with the author, 27 February 2006.

experimentation with therapeutic access and pastoral care, such a linkage is less likely to figure in the calculations of the CROs, especially those focused on early-stage trials, since their source of value lies directly in increasing the number of trials they can conduct, rather than in providing tangible therapeutic benefits to patients. As suggested earlier, it is the CRO industry rather than physicians that is currently driving the establishment of regulatory infrastructure in India. The Delhi-based psychiatrist told me that while there is intense debate within the psychiatric community in India over the relationship of clinical trials to drug access, physician investigators are involved only to a very limited extent in efforts to streamline the regulatory process.

This subjection of patients to experimental regimes without an insistence on concomitant therapeutic access does not seem to arise primarily from any reluctance of Western pharmaceutical companies to market drugs in India. It is true that 85 per cent of all global drug sales are currently accounted for by US, European and Japanese markets, though the burgeoning middle class in India may be a factor in the companies' future planning. At the present time, however, the only real avenue for any sort of therapeutic access to experimental drugs is through the 'compassionate use' programmes of a number of pharmaceutical companies, which make the drugs tested in Phase 3 trials available to the sick volunteers for a fixed period of time after completion of the trial. No one in the Indian CRO industry whom I talked to, and no one who is actively involved in developing clinical-practice guidelines, felt it was necessary to insist that drugs tested in India should be marketed there, in contrast to the vigorous discussion among physicians of the relationship between clinical trials and access to drugs. 'Ethics', therefore, are provisional and partial, bearing primarily at this point on concerns about informed consent.

The uncoupling of experimental subjectivity from therapeutic access, which—through acts of omission—occurs at a legal and regulatory level, enrols Indian experimental subjects in the cause of health, but locates them outside a regime of pastoral care. In other words, these experimental subjects contribute in some nebulous sense to health by making themselves available as experimental subjects, but this is in no way necessarily linked to their own healthiness, or that of other Indians who might obtain access to new medication as a consequence of the risks to which the volunteers are exposed. The nature of these risks was brought home to me during my tour of Vimta, when I was shown a room, at the

time dark and secluded, with just four beds in it. This, I was told, is the intensive care unit where trial subjects are admitted and ministered to in case of adverse effects. It looked like a medical emergency room of the kind used to attend to accidents on the factory floor. It re-emphasized not just the high-risk nature of experimental subjectivity, but that being a trial subject is, specifically, high-risk *labour*.

3. EXPROPRIATION, EXPLOITATION, VIOLENCE

A theoretical critique of the global biomedical economy, situating the latter in relation to the logics of expropriation and exploitation, requires the introduction of the key concepts of *biocapital* and *surplus health*. By biocapital, I refer to the simultaneous systemic and emergent production of the life sciences, especially biomedicine, alongside the frameworks of capital and the market within which such technoscience increasingly operates. There are three layers of specificity to biocapital: institutional, epistemic and structural/epochal.

First, the biomedical industry, like any other, has its specific institutional terrain. In the US, this terrain is seen as partitioned into ‘upstream’ and ‘downstream’. Downstream lie big multinational pharmaceutical companies, with the human and capital resources to bring drugs to market. These are supplemented by a few biotech companies that have managed to grow sufficiently to join the marketing effort. Upstream companies conduct more basic research, focusing on informatics, the development of diagnostic kits or the provision of research tools to other companies. Clinical-research organizations fit into this model as downstream facilitators to large pharmaceutical companies. There are particular risks in this marketplace, in view of the enormous time spent on drug development (roughly fifteen years), the cost (\$800 million per drug, according to the industry, though that is most certainly inflated) and the risk (only one in five drugs makes it through clinical trials). And there are particular power hierarchies within it, such as the hugely powerful position of big pharmaceutical companies in the value chain relative to smaller biotech companies.

The second layer of specificity is epistemic. For instance, emergent life sciences such as genomics have the potential to radically reconfigure our understanding of life in ways that parallel the fashion in which

neo-liberal logics of capital are reconfiguring our understanding of value.¹⁸ While I do not elaborate on this point here, I believe that to describe the institutional arrangements of the life sciences is not a sufficient basis for comprehending biocapital in all its complexity; emergent epistemologies are also crucial.

These first two layers of specificity are internal to biocapital. The third has to do with the larger epochal transformations in capitalism as a whole, which preface some of biocapital's structural logics. The transformation that is pertinent to understanding biocapital is what Joseph Dumit identifies as the change in the logic of the biomedical industry, shifting away from being 'an arm of capital' to becoming 'an industry in itself'.¹⁹ At an earlier stage of capitalist development, medicine was integral to reproducing the conditions under which industrial production was made possible. Capital needed healthy workers. But just as the logic of commodity production became self-perpetuating and self-sustaining, to the point where commercial activity became an end in itself, so too has the logic of the production of health for work become self-perpetuating and self-sustaining, turning into an industry that produces health not for work's sake, but for health's sake. In biocapital, health operates directly as an index of value, unmediated through the labour-power of the worker. In Foucauldian terms, it is not labour but life itself which becomes the locus of value in biocapital, with health becoming the index of life, rather than the facilitator of labour.

Crucial to this transformation is the emergence of the value-form of surplus health. Dumit defines surplus health as 'the *capacity* to add medications to our life through lowering the level of risk required to be "at risk"'.²⁰ This occurs by setting biomedical risk thresholds. Clinical trials become a part of the apparatus through which such a lowering of the risk level takes place. An analogy might be made with the way in which machinery, in Marx's analysis in Volume One of *Capital*, operates not to reduce work, but to increase surplus labour by widening the gap between waged work and the potential productivity of the worker.

¹⁸ For a more extensive elaboration of this logic, see Melinda Cooper, *Surplus Life: Biotechnics and the Transformation of Capital*, Seattle forthcoming.

¹⁹ Joseph Dumit, 'Drugs, Algorithms, Markets and Surplus Health', *Lively Capital* workshop paper presented at University of California, Irvine, 2006.

²⁰ Dumit, 'Drugs, Algorithms, Markets and Surplus Health'.

Surplus health refers to the market value that pharmaceutical companies gain from the potential for future illness of those who might one day consume their drugs—which includes anyone with the buying power to constitute a market for therapeutics. As with surplus-value in the Marxian sense, surplus health is an animating abstraction, in this case of the logic of pharmaceutical risk. Just as the setting of wage rates is the material calculus for the unfolding of surplus-value, so the setting of biomedical risk thresholds is the material calculus upon which surplus health unfolds. And as machinery serves to increase surplus-value by increasing the potential for labour over and above that remunerated by wages—through an increase in the *efficiency* of labour—so too can clinical trials serve to increase surplus health by demonstrating therapeutic efficacy.

Similarly, just as machinery requires labour to operate it—which, during the era of industrial capital, was high-risk work—so clinical trials require experimental subjects as their high-risk labour. Dumit suggests that biomedical markets in advanced liberal societies—especially the United States—depend on the generation of surplus health, which in turn operates through the setting of risk thresholds. The knowledge of disease risk provided by diagnostic-testing capabilities, and calibrated through these thresholds, enables the marketing of drugs for diseases that are increasingly reframed as ‘chronic’. Just as much of the manufacturing labour previously performed by the working class in the First World was later exported to Third World peripheries, so much of the Phase I experimentation, initially performed on marginal populations in the US, is now being exported to Third World sites such as India. The experimental subjects there, outside the circuits of pastoral care and therapeutic consumption, come to be *merely risked*. But these very circuits rely for their constitution on the existence of such ‘merely risked’ subjects. These experimental subjects provide the conditions of possibility for the neo-liberal consumer subjects for whom surplus health is generated.

The context of consent

The ‘merely risked’ volunteer is subjected to a logic of expropriation integral to the structural logic of biocapital that I am trying to trace. Bodies are made available to the global machinery of experimentation, machinery driven by the value logic of pharmaceutical capital. Indeed,

the global scale of these circuits is precisely a function of capital's value considerations. Without the cost rationales for outsourcing clinical trials to the Third World, their globalization would not have become such a dynamic imperative—such trials had, after all, been an important part of the American drug development landscape for nearly half a century before moves to take them abroad began in the mid 1990s. And without the property mechanisms, harmonized and enforced globally through the WTO, that provide patent protection to multinational pharmaceutical interests, globalizing capital would not have had the security to realize its aspirations. Similarly, capital considerations drive the Indian CRO industry to a vigorous build-up of infrastructure to attract clinical trials, increase trial recruitment, and uncouple these considerations from any serious concern with therapeutic access.

In this situation, the partial ethic enshrined in 'good clinical practice', far from mitigating the structural violence of capital, serves instead to facilitate it. The instrument through which this takes place is the liberal contract embodied in the informed consent form. Just as the wage is the materialized contractual form through which individuals are 'freed' from serfdom and converted into workers for industrial capital, so the informed consent document 'frees' experimental subjects from being coerced guinea-pigs by providing them with the autonomous agency such a contract signifies. The concerns raised over ethical variability in global clinical trials are often premised on the notion that ethical enforcement is likely to be looser in the Third World than in the First. My attempt here has been to show that, on the contrary, it is precisely the global harmonization of ethical standards that provides the conditions of possibility for the experimental subjection of the 'merely risked' Third World subject; and further, that this harmonization of ethics goes hand-in-hand with the global harmonization of property regimes. These two parallel movements—the contractual codification of ethics and the exclusionary instruments of property—together provide global capital with the security to turn healthy Indian populations into experimental subjects, who are both merely risked and free to choose to be so.

The structural violence of clinical experimentation starts with the fact that it is a procedure that can only be set in motion by the risking of healthy subjects. Indeed, the very epistemology of clinical trials is risk-laden—both for the subjects experimented upon, and for the companies who invest huge amounts of money in a therapeutic molecule

that may or may not eventually come to market. The structural violence of experimentation is then exacerbated by pre-existing global inequalities, which result in more bodies available for less cost in Third World locales. If the former violence is epistemic, the latter is historical. A third layer of structural violence is imposed in the form of the liberal contract, which frees the experimental subject to make his body available not just for experimentation, but for exploitation, since the clinical trial becomes a locus of surplus-health generation.

The question raised by this third layer of structural violence is one that was central for Marx in his analysis of capital, and pertains to the conditions of possibility that ensure the availability of workers for capital—or in this case, of experimental subjects for clinical trials—in the first place. In ‘The So-Called Primitive Accumulation’, Marx shows that this availability is generated by pre-existing acts of violence that created a property-less proletariat.²¹ Such processes are historically specific, but they do show a consistency of form. Thus, for instance, subject recruitment into Phase I clinical trials in India occurs, on the face of it, through newspaper advertisements. The public face of trial recruitment does not, however, reveal the conditions that make it financially attractive for individuals to risk themselves as experimental subjects.

I have written elsewhere, for example, about Wellquest, which is located in the mill districts of Mumbai.²² I learned from scientists there that most of the trial subjects recruited by this CRO happened to be unemployed mill workers who had lost their jobs due to the progressive evisceration of the Mumbai textile industry over the last thirty years. The number of unemployed is over two hundred thousand, many of whom are still waiting for the payment of back wages. They are already, therefore, subjected to the violence of de-proletarianization that occurred following the demise of a sector of manufacturing capital. This violence is exacerbated by the fact that the textile mills are situated on prime land for property development, with former mill owners themselves turning to real-estate speculation as a far more lucrative source of capital investment. This means that the workers’ tenements or *chawls*, mainly

²¹ Karl Marx, *Capital: A Critique of Political Economy, Volume One*, translated by Ben Fowkes, Harmondsworth 1976.

²² Sunder Rajan, ‘Subjects of Speculation: Emergent Life Sciences and Market Logics in the US and India’, *American Anthropologist*, vol. 107, no. 1 (2005), pp. 19–30. See also *Biocapital*, Chapter 2.

located close to the mills, are under threat of demolition, so that in addition to losing wage and livelihood, these workers are now in danger of losing their shelter as well. Demolition of the *chawls* was temporarily halted by a 2005 Bombay High Court verdict that stayed real-estate development in the mill districts, but this was overturned by the Indian Supreme Court in March 2006, making it legal to tear down the mills and *chawls* and build middle-class housing instead.

The violence of de-proletarianization and dispossession is a function of the dominance of speculative real estate, which has replaced textile manufacturing as a source of value-generation for capital. A number of unemployed mill workers have turned into street hawkers in order to earn a living, but there is an organized state and middle-class campaign against the hawkers, who are deemed noisy and polluting, and perhaps most importantly, accused of taking up valuable parking space.²³ There is no way to understand the dynamics of clinical experimentation in the mill districts of Mumbai without taking into account all these prior moments of violence that provide the inducement to sign an informed consent form. First the mill workers are removed from their factories. Then they are removed from their dwellings. Then they are removed from the streets. Only thus do they acquire the freedom to become autonomous trial ‘volunteers’.

Global connections

One way of understanding the situation of expropriation that I have described is in terms of neo-colonialism. This is the trope employed by Nundy and Gulhati in their critique of clinical trials in India. It is also consonant with positions taken in various fictional portrayals of ‘bio-colonialism’, such as Manjula Padmanabhan’s dystopian play *Harvest*, or Patricia Grace’s *Baby No-Eyes*.²⁴ All these accounts portray a deep historical and continuing inequality, whereby rich/First World/white subjects enrich their health—and often wealth—through the corporeal dispossession of subaltern/Third World/racially marked subjects. While sympathetic to the inequalities that such accounts describe, the

²³ For an account of the violence against hawkers in Mumbai, see Arvind Rajagopal, ‘The Menace of Hawkers’, in Katherine Verdery and Caroline Humphrey, eds, *Property in Question: Value Transformation in the Global Economy*, Oxford 2004.

²⁴ Manjula Padmanabhan, *Harvest*, London 2003; Patricia Grace, *Baby No-Eyes*, Honolulu 1998.

accumulation by dispossession, to use David Harvey's term,²⁵ that I am trying to trace here is not agential but structural, where the one thing that accumulates as a consequence of 'merely risking' experimental subjects is not health—not even that of the advanced liberal subject—but value.

For this, it is important to turn to Dumit's account of surplus health in the United States. The therapeutic economy that Dumit traces in the US context is also not one of pastoral care, but rather therapeutic saturation. Dumit and I have indeed suggested that, considered from the perspective of pharmaceutical company logic, health in the US is not about healthiness either, but about expanding the market for therapeutics.²⁶ Rising therapeutic consumption can be achieved either by increasing the number of people who take a particular drug—most effectively achieved by 'off-label use', i.e. prescribing drugs for treatments other than those for which the drug was initially approved—or by increasing the time-span of the prescription, justified by reframing diseases as chronic states rather than events. Dumit observes that currently 'the average American is prescribed and purchases somewhere between nine and thirteen different prescription-only drugs per year.' He continues:

According to the pharmacy benefits companies and insurance companies, such as Express Scripts, sampling 3 million unique individuals in their plans, 11 per cent of Americans were prescribed cholesterol-lowering drugs last year, 40 per cent of all those over 50. More than 20 per cent of women over 40 were prescribed anti-depressants in 2002, almost 10 per cent of boys 10–14 were prescribed attention-deficit disorder drugs . . . The growth rates for almost all classes of drugs have been in the low double digits for a decade, with prescription rates for children growing upwards of 30 per cent per year. Similarly, both the prevalence (the number of people on each drug) and the intensity (the size of the yearly prescription) are projected to continue to grow in all drug categories for the foreseeable future. The figures do match the fears, and according to many surveys, Americans are spending more time, more energy, more attention, and money on health. Health clearly is not simply a cost to the nation to be reduced; it is also a market to be grown.²⁷

²⁵ David Harvey, *The New Imperialism*, Oxford 2003.

²⁶ Joseph Dumit and Kaushik Sunder Rajan, 'Biocapital, Surplus Health and the End(s) of Biopolitics', manuscript in preparation.

²⁷ Joseph Dumit, 'Living in the Aggregate: Accumulating Prognoses, Growing Markets, Experimental Subjects'. Paper presented at American Anthropology Association meeting, San José, 2006.

Marx's analysis in Volume One of *Capital* is two-fold. First, the contemporary conditions of industrial capital that he traces are marked by exploitation materialized through surplus-value, a function of labour-power being always already greater than the labour remunerated by wage. Analogously to this, surplus health is a function of potential therapeutic consumption that is always already greater than that required to maintain healthiness. This excess therapeutic consumption is not harmless—indeed, it involves ever-greater medication of the American population, and has produced catastrophic and fatal side-effects such as those associated with the cox-2 inhibitor Vioxx. This therapeutic saturation also leads directly to biomedical rationalizations for the outsourcing of clinical trials, as it becomes increasingly difficult to test the effects of experimental drugs in populations who tend to be on many other drugs that interact with the molecules being tested.

But the conditions of possibility for exploitation through surplus-value generation are, as Marx shows, dependent on a prior expropriation, achieved through a form of violent accumulation that forces people into becoming workers for industrial capital in the first place. The two-fold movement of capital—violent dispossession followed by exploitation—is a temporal one in Marx's analysis. In the case of clinical trials, however, the violence is spatial, with Third World experimental subjects expropriated not so that First World consumer subjects become healthy, but so that they can be exploited. In both cases, the only value that is constantly preserved and increased is value itself.

Much of my argument rests on the fact that clinical experimentation in the Indian context is not linked to therapeutic access. It is, however, certainly possible to imagine such a situation; and if this linkage is not created either by the intervention of advocacy groups fighting for access to drugs, or by the state's insistence on a biopolitical rationale of public good and public health, it is most likely to be brought about by market mechanisms once India is perceived as a potential market for therapeutic consumption. In such a scenario, one can quite easily envisage the continued expropriation of experimental subjects—those who fall out of the market because they lack the purchasing power to buy drugs—side by side with exploitation of therapeutic consumers within India itself. Stefan Ecks has been studying psychiatric drug marketing by companies

like Pfizer in India, and observed strategies not dissimilar to those employed in the US.²⁸

If we are to understand biocapital from the perspective of the pharmaceutical companies' logic, then what is at stake is not therapeutic access in the cause of health, but increasing therapeutic consumption in the cause of value. In parallel, from the perspective of CROs, the issue is not clinical trials in the cause of therapeutic access, but rather clinical trials in the cause of value. The global articulation of pharmaceutical and CRO logics of value-generation both structures and overdetermines an allegedly benign enterprise in terms of expropriation and exploitation. Other competing logics of capital also naturally come into play, most notably a logic of insurance that is particularly salient in the American context of managed care. It is also relevant to the European public-health context, where paying for increased therapeutic consumption is a burden, and the logic of value dictates an accent on disease prevention that is not mediated by therapeutic saturation.

It is important in every case to privilege the analysis of value, rather than assuming from the outset that the issue is one of biopolitics or pastoral care. At the same time there are many incongruities that are vital to note, not least the Indian state's hyper-attentiveness to ethics and its regulation of clinical practice. The structural violence of global clinical trials on the subcontinent is not due to a lack of ethics, but to the fact that value, captured by the logic of capital and mediated through the pharmaceutical and CRO industries, overdetermines the practices that emerge.

²⁸ Except that direct-to-consumer advertising, an important strategy in the US, is not allowed in India. Instead, such marketing is aimed exclusively at physicians. Stefan Ecks, 'Global Citizenship Inc: Big Pharma and "Depression Awareness" in Urban India', *Asian Biotechnologies* workshop paper presented at Honolulu, 2006.