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# Big-pharmaceuticalisation: Clinical trials and Contract Research Organisations in India

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ABSTRACT

The World Trade Organisation's Trade Related Intellectual Property Rights [TRIPS] agreement aimed to harmonise intellectual property rights and patent protection globally. In India, the signing of this agreement resulted in a sharp increase in clinical trials since 2005. The Indian government, along with larger Indian pharmaceutical companies, believed that they could change existing commercial research cultures through the promotion of basic research as well as attracting international clinical trials, and thus create an international level, innovation-based drug industry. The effects of the growth of these outsourced and off-shored clinical trials on local commercial knowledge production in India are still unclear. What has been the impact of the increasing scale and commercialisation of clinical research on corporate science in India?

In this paper we describe *Big-pharmaceuticalisation* in India, whereby the local pharmaceutical industry is moving from generic manufacturing to innovative research. Using conceptual frameworks of pharmaceuticalisation and innovation, this paper analyses data from research conducted in 2010–2012 and describes how Contract Research Organisations (CROs) enable outsourcing of randomised control trials to India. Focussing on twenty-five semi-structured interviews CRO staff, we chart the changes in Indian pharmaceutical industry, and implications for local research cultures.

We use *Big-pharmaceuticalisation* to extend the notion of pharmaceuticalisation to describe the spread of pharmaceutical research globally and illustrate how TRIPS has encouraged a concentration of capital in India, with large companies gaining increasing market share and using their market power to rewrite regulations and introduce new regulatory practices in their own interest. Contract Research Organisations, with relevant, new, epistemic skills and capacities, are both manifestations of the changes in commercial research cultures, as well as the vehicles to achieve them. These changes have reinvigorated public concerns that stress not only access to new medicines but also the 'price' of innovation on research participants.



## 1. Introduction

India signed the World Trade Organisation's [WTO] Trade Related Intellectual Property Rights [TRIPS] agreement in 1995. This agreement aimed at harmonising intellectual property rights and patent protection globally. India's decision to sign was controversial: civil society activists were convinced that this would reduce Indian people's access to cheap drugs, and many representatives of India's generics drug companies feared the loss of their right to reverse-engineer products that were patent-protected elsewhere in the world through a process that involves the separation, identification and precise estimation of quantities of ingredients in a formulation, for characterization of a competitor's product and the development of a generic alternative (Ramanna, 2003). While a few large-scale companies and most small-scale generics companies

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remained opposed, most Indian large-scale producers welcomed the opportunity to access high-income markets, and the prospect of becoming innovator companies themselves (Smith, 2000). Signing the TRIPS agreement required changes to the 1970s Patent Act that provided Indian companies the same protection for their innovations as companies elsewhere, encouraging them to shift their focus from production of generic drugs to innovation of New Chemical Entities (Schüren, 2013). During the 1995–2005 grace period, for example, the Indian pharmaceutical companies Dr Reddy's and Ranbaxy were able to secure patents on novel compounds and venture out to international markets with them (Chaturvedi and Chataway, 2006).

Extending patent protection to drugs produced in India is, however, but one side of the story of pharmaceuticalisation. One important result of this process has been an increase in the quest for new markets and drug products that has led to an expansion of research organisations, and created new social actors. Legislative changes to implement TRIPS in India made possible not only increased access by innovator companies to the Indian market, but also the introduction of internationally-funded clinical trials. A change in Schedule Y of the Indian Drugs and Cosmetics Act in 2005 removed a phase-lag on clinical trials: pharmaceutical companies could now 'conduct trials of new drugs in India at the same time that trials of the same phase are being conducted in other countries' (Nundy and Gulhati, 2005: p.1633). Data on clinical trials published in the *Indian Journal for Medical Ethics* show an increase from 64 new trials in 2006 to 245 in 2010 (Ravindran et al., 2010) and up to 787 in 2012 (Ravindran and Vaid, 2013), suggesting a 1100% increase in 6 years. However, on global scale India held only 1% clinical trials in 2007 (Thiers et al., 2008). Indian companies also increased their own clinical trials, testing new chemical entities of their own and entering into contracts with international companies. The growth in clinical trials activity allowed innovator companies to sponsor trials both directly and through Contract Research Organisations [CROs] (Drabu et al., 2010; Yee, 2012). The impacts of TRIPS agreement on patent laws and on the encouragement of clinical trials seemingly pull in different directions, but that they are in fact enmeshed processes. This very particular trajectory of pharmaceuticalisation deserves to be unpicked in detail: how have these transformations in the terms of market competition changed research cultures? The significant role played by CROs in enabling this process is the central focus of this paper.

The pharmaceuticalisation thesis has evolved out of the work of Abraham (2010, 2011; also see Davis and Abraham, 2013), and Williams et al. (2011) who suggest that, at the most basic level of the definition, drugs are increasingly seen as pre-eminent solutions to health problems. Abraham argues that drivers of pharmaceuticalisation include 'the redefinition of health problems' and 'changing forms of governance' and note that 'pharmaceutical industry marketing, consumerism, and the ideology of the "expert patient" are important factors in the process (Abraham, 2010). Williams et al., (2011, p.719) stress in addition that 'pharmaceutical futures are shaping how we think about innovation, policy and the very meaning of health and illness, therapy and enhancement', largely referring to pharmacogenomics and its potentials. This debate has, firstly, been carried out largely as a discussion of changes within 'Western' societies: India appears merely as a source of cheap pharmaceuticals. Secondly, it has failed to take seriously the globalisation of particular kinds of pharmaceuticalisation as part of an emergent neo-liberal market form and associated discourses and practices. Here, we argue that India (perhaps more clearly than elsewhere) is experiencing 'Big-pharmaceuticalisation'. By this we mean the following:

a. TRIPS has encouraged a concentration of capital, with large companies gaining increasing market share and using their market power to rewrite regulations and regulatory practices in their own interest;
b. New social forms associated with these changes have been introduced into India – international multi-sited clinical trials and Contract Research Organisations, and have developed new epistemic skills and capacities, as well as regulatory frameworks and practices;
c. Public contests have been reinvigorated over the well-being of local populations, be they concerning access to pharmaceuticals or the health of trial participants. Concerns stress not only access to new patented medicines but also the 'price' of innovation on research participants, and the regulatory structures that should govern clinical trials and research participation.

Pharmaceuticalisation describes how drug production and manufacturing, along with their sales, branch out to ever more widening global regions (Abraham, 2010, 2011; Bell and Figert, 2012; Williams et al., 2011, 2012). A substantial literature analyses the introduction of clinical trials into developing countries and emerging economies (Kamat, 2014; Petryna, 2009; Sariola and Simpson, 2011; Sunder Rajan, 2005). We extend the definition of pharmaceuticalisation to include the globalisation of pharmaceutical knowledge production by means of clinical trials. Petryna (2009) describes how when CROs 'go global', they work across national and cultural boundaries, spread the methodologies, skills and ideas of the pharmaceutical sector, and facilitate the increase in clinical trial activity in countries like India, China and Brazil. We agree with other analysts of commercial research and pharmaceuticals that such clinical trials ought not be considered 'science' but rather a mechanistic, pre-defined test (Bachelard, 1953, quoted in Gaudilliere and Löwy, 1998, p.10; Cooper, 2012).

Changes within these new locations, and how existing practices are morphed into new settings, need further analysis. When international pharmaceutical companies outsource trials in search of new markets and treatment-naïve patients, they transform the existing pharmaceutical sector, harmonising it to resemble more closely international or 'Big Pharma'. Big-pharmaceuticalisation involves the introduction of CROs, who implement research for international and national pharmaceutical companies, into India. Working with sponsors, doctors on trial sites where patients are recruited, and at times biotechnology companies doing basic research, CROs are actors in their own right. They reinforce how Randomised Control Trials (RCTs) become central to a particular form of knowledge production, and begin to displace pre-existing generic drug production regimes. Thus, Big-pharmaceuticalisation stands for both the arrival of CROs, trials, and the new social forms – regulatory and human capital – that come with them, as well as the process through which India is becoming more like the international sector. CROs are both vehicles and manifestations of this change.

The TRIPS agreement subverted the past reverse-engineering policy, as innovative products can now be patented in India and international companies can include India in multi-sited trials. Arguments concerning these changes are polarised. Innovation-management literature sees them as economic opportunities for the industry (Chataway et al., 2007; Chaturvedi and Chataway, 2006; Chittoor et al., 2009; Gehl Sampath, 2007; Kale, 2009, 2010; Kale and Little, 2007; Kale and Wield, 2008). Others argue that therapeutic access, patients' rights, and the state's responsibilities in health care provision for its citizens are all threatened. India's new Patents Act has clauses that include public health concerns as reasons to deny a patent. They are designed to check 'ever-greening', whereby drug companies exploit legal