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Pharmaceuticalisation and ethical review in South Asia: Issues of scope and authority for practitioners and policy makers

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ABSTRACT

Ethical review by expert committee continues to be the first line of defence when it comes to protecting human subjects recruited into clinical trials. Drawing on a large scale study of biomedical experimentation across South Asia, and specifically on interviews with 24 ethical review committee [ERC] members across India, Sri Lanka and Nepal, this article identifies some of the tensions that emerge for ERC members as the capacity to conduct credible ethical review of clinical trials is developed across the region. The article draws attention to fundamental issues of scope and authority in the operation of ethical review. On the one hand, ERC members experience a powerful pull towards harmonisation and a strong alignment with international standards deemed necessary for the global pharmaceutical assemblage to consolidate and extend. On the other hand, they must deal with what is in effect the double jeopardy of ethical review in developing world contexts. ERC members must undertake review but are frequently made aware of their responsibility to protect interests that go beyond the 'human subject' and into the realms of development and national interest [for example, in relation to literacy and informed consent]. These dilemmas are indicative of broader questions about where ethical review sits in institutional terms and how it might develop to best ensure improved human subject protection given growth of industry-led research.

From time to time, terms appear in the social sciences which help in capturing a biomedical *zeitgeist*. Notions such as 'medicalization' and 'geneticisation' (Lipmann, 1991; Hedgecoe, 1998; Have, 2001) have in the past provided a simple shorthand for the ways that social, economic and technological changes begin to reshape the landscape of health care and the experience of those that pass through it. In similar fashion, pharmaceuticalisation has entered social science discourse. Williams et al. (2011) provide a critical evaluation of this concept and its utility in understanding the pervasive impact of pharmaceuticals within medical systems, economies and societies (also see (Abraham, 2011)). Consistent with their intention to give greater specificity to the pharmaceuticalisation thesis, we set out in this article to interrogate some of the 'upstream (macro) level processes' (2011: 712) that come within the ambit of pharmaceuticalisation. The arena we consider is one which is increasingly important in understanding the growth and development of pharmaceuticals in society but one that is often lost in a bias towards Euro-American accounts of this process. Here we bring together globalisation, governance and the ethical review of clinical trials involving human subjects in the developing world. The main sites we consider are research ethics committees and the responses of their members to a growing number of protocols for industry-sponsored clinical trials. What we show through this analysis is the way that the growing engagement with pharmaceutical interests across South Asia produces significant tensions for ERC members. Beneath the documentary and procedural claims to standardised measurement, rules and disinterested evaluation in ethical review, industry-sponsored clinical trials generate concerns about scope, legitimacy and authority for those whose job it is to undertake and develop credible ethical review (*cf* Timmermans and Almeling, 2009; Timmermans and Epstein, 2010). Whilst such tensions are likely to be evident in any context where research

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ethics and economic interest coalesce, we argue that in developing world settings there are other factors in play that give these questions a particular urgency and complexity.

Our stepping off point in considering the relationship between ethical review and clinical trials in South Asia is a question posed by Rachel Douglas–Jones in her doctoral thesis on capacity-building in ethical review in Asia: 'what are the problems to which the ethics committee is a solution?' [2013, p34]. The question is an important one. Ethical review committees play a crucial role in the regulation of experimentation involving human beings. In the most basic of terms, the approval of a formally constituted body of experts should ensure that research is beneficial, scientifically valid, and, above all, safe for those who participate. Yet, whereas in Europe and North America ERCs may have reached a degree of institutional integration and stability, they are still very much in a state of development in parts of the world that have only recently been drawn into the rapidly growing demand for experimentation involving human subjects. South Asia is a case in point. Capacity for ethical review is rapidly developing across the region and ERCs currently follow a broadly similar institutional and procedural format. Regional capacity-building has developed in association with organisations like the Forum for Ethical Review Committees in Asia and the Western Pacific (FERCAP), the Strategic Initiative for Developing Capacity in Ethical Review (SIDCER) and the Global Forum on Bioethics (GFB) all of which work to build capacity when it comes to the review of projects locally. Affiliation to these organisations and the establishment of local branches [for example, FERC – Sri Lanka and FERC – India] is an important route to harmonisation and the dissemination of good practice. Arguably however, the more powerful source of standardisation for review of industry conducted trials has been the ICH-GCP guidelines which aim to provide 'a more economical use of human, animal and material resources, and the elimination of unnecessary delay in the global development and availability of new medicines whilst maintaining safeguards on quality, safety and efficacy, and regulatory obligations to protect public health' (ICH, 2005). Drawing on a genealogy of crisis reaching back to the Declaration of Helsinki, the ICH-GCP lays down detailed benchmarks for the ethical and scientific conduct of trials. Yet, linking the work of ERCs with a genealogy of universal human rights in this way provides significant cover for the extension of commercial pharmaceutical research (Abraham, 2007; Abraham and Reed, 2002). In this view, ERCs are the handmaiden rather than the governor of trial activity with ethical review seen as essentially procedural, bureaucratic and rule observing. Earlier studies suggest that in countries that have embraced standard guidelines and particularly the ICH-GCP guidelines, ERCs are apt to operate in ways that appear to be more about legal defence of researchers rather than actual protection of subjects (Bosk, 2007; Kleinman, 1999; Stark, 2012). Our analysis confirms these concerns, and shows ethics committee members raising issues that are not limited to human subject protection *per se* but drawing in a range problems which afflict large numbers people in their society [for example, poor access to resources, corruption, illiteracy, inequality to name but a few]. These issues are articulated at a variety of scales [the person, the hospital, the University, the research community, the vulnerable, the nation state, the developing world and so forth]. Yet, the reality faced by many ERC members is one of growing pressure to accomplish human subject protection by narrowing the focus of ethical review such that it is clearly in line with industry specified guidelines.

1. Methods

The data on which this paper is based are drawn from a study of the growth of clinical trials and human experimentation in South Asia [India, Nepal and Sri Lanka].[1] In this study we identified key actors in the conduct, management and regulation of clinical trials in a variety of settings (See Table 1).

Table 1
The BHESA interview data-set.

Category	Nepal	India	Sri Lanka	US, UK	Total
PIs and Co-Is	10	31	11	3	55
Clinical research assistants	14	18	11	0	43
Other trial staff	24	22	39	0	85
Collaborators	0	3	1	1	5
Sponsors and CRO staff	0	35	1	13	49
Ethics committee members	6	14	6	0	26
Regulators	2	7	2	6	17
Other key informants	17	18	9	13	57
Total	73	148	80	36	337

In total we carried out 337 semi-structured interviews, the vast majority of which were recorded, translated into English where necessary, and transcribed. The resulting dataset was entered into Atlas.ti for coding. The codes were generated by an iterative process at a workshop held in Mumbai with all coders present; trial codings were carried out and a selection of interviews was recoded to ensure consistency.

Here we draw principally on extended interviews with a small sub-set of Ethical Review Committee [ERC] members from India [14], Sri Lanka [6] and Nepal [6]. In many respects, the sample is unrepresentative of the wider body of reviewers at work in each of these countries as it was self-selecting and therefore tended to be made up of people who were knowledgeable, articulate and keen to express their views on the rights and wrongs of clinical trials, the work of ERCs and their less responsible colleagues. They were also mostly from Institutional [hospital] and University settings. Nonetheless, consideration of their accounts of topics such as ethical review, operation and composition of committees, capacity building, training for reviewers and approaches to informed consent provides a useful indicator of the major challenges faced by committed ERC members in the settings identified. We also draw to a lesser extent on interviews with regulators, policy-makers, academics and investigators involved in developing ethical review infra-structure. Before considering these responses in detail it is necessary to consider briefly the three contexts in which our study took place.

2. India

India has a well-established pharma industry dating back to the 1950s. The thrust of this industry has been the production of generics for local markets. This infrastructure, combined with large numbers of English speaking doctors and technicians, as well as large populations of treatment naive people with a range of disorders of interest in the west [e.g. cancers, cardio-vascular disease, diabetes] has stimulated much interest in clinical trials. Trials are outsourced by western pharmaceutical industries as well as conducted by local companies keen to move into global markets for their products. Acceleration in this sector of activity has overwhelmed existing machinery for ethical review and monitoring which previously catered mostly for locally conducted research. Along with Ethical Guidelines for Biomedical research Involving Human Subjects Indian Council of Medical Research (2000), the

[1] The research was funded by the Economic and Social Research Council of the United Kingdom in collaboration with the Department for International Development [ESRC/DfID nbrRES-167-25-0503]. Ethical approval for the study was initially given by the School of Social and Political Sciences Research Ethics Committee, University of Edinburgh [13/10/2010]. Ethical clearance was then gained from local ERCs for research to be carried out in India, Nepal and Sri Lanka.