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Ethical Issues in Outsourcing: The Case of Contract Medical Research and the Global Pharmaceutical Industry

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Abstract The outsourcing of medical research has become a strategic imperative in the global pharmaceutical industry. Spurred by the challenges of competition, the need for speed in drug development, and increasing domestic costs, pharmaceutical companies across the globe continue to outsource critical parts of their value chain activities, namely contract clinical research and drug testing, to sponsors across the globe, typically into emerging markets. While it is clear that important ethical issues arise with this practice, unraveling moral responsibility and the allocation of responsibility is not so clear, considering that contracts, by their very definition transfer responsibility from the principal to the agent. This research provides a framework for exploring some of the ethical issues, including attributions of moral responsibility associated with Contract Medical Research. Using a theory of strategic and moral behavior, the research shows that both clients and sponsors in contract research have individual and collective responsibility to ensure that due care and diligence is exercised in the performance of clinical research. The research suggests some guidelines for stakeholder action.

Keywords Outsourcing · Ethics · Moral theory · Moral responsibility · Contract research · Corporate social responsibility

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Introduction

The outsourcing of medical research has become a strategic imperative in the global pharmaceutical industry. Spurred by the challenges of competition, the need for speed in drug development, and increasing domestic costs, pharmaceutical companies across the globe continue to outsource critical parts of their value chain activities, namely clinical research and drug testing, to sponsors across the globe, typically into lower-wage, emerging market countries.

By its very nature, medical research has ethical implications and the ethical issues associated with medical research may be compounded when the function is outsourced, especially to emerging markets that have generally weak institutional environments. This research focuses on the ethical issues associated with the outsourcing of medical research, Contract Medical Research (CMR) to Contract Research Organizations (CROs) in emerging markets. CROs are commercial entities that perform clinical trials for pharmaceutical companies. The very nature of CMR outsourcing, notably the presence of multiple stakeholders (pharmaceutical companies who are the clients, CROs who are sponsors, governments who provide the regulatory environment, and individual researchers who end up conducting the studies), leads to a progressive diffusion of responsibility. This diffusion of responsibility may make it more difficult to assign accountability when there is some ethical malfeasance in CMR. Indeed, while CMR allows client firms to transfer legal responsibility to sponsors, issues of moral responsibility for sponsor and third party acts of omission and commission remain unresolved. While it is clear that contracts transfer legal responsibility and culpability, the transferability of moral responsibility and behavior, the *locus classicus* of ethics,

are more complex. Thus, a critical issue is to explore who bears moral responsibility for the integrity of outsourced medical research. Our understanding of this and similar issues may be important for assigning responsibility for corrective action. This research provides a framework for exploring some of the ethical issues associated with outsourcing medical research into emerging economies, including issues of moral responsibility and corrective action.

This article is organized as follows. First section presents a brief discussion of the motivations and facilitating conditions for CMR in the global pharmaceutical industry. Second section presents a discussion of key contextual factors associated with CMR. These factors include the nature of CMR, its governance, sponsor and client focus on cost minimization and the implications for behavior. Third section presents a detailed discussion of moral responsibility, including the allocation of moral responsibility in CMR outsourcing. Building on moral psychological theories on attribution of moral responsibility (see for example, Driver 2008; Alicke 1992), it is argued that when ordinary, commonsense attributions of responsibility are applied, pharmaceutical companies may assume blame even if they are not the direct causes of unethical behavior in CMR outsourcing. Fourth section presents the moral and strategic imperatives for action. Fifth section provides guidelines for corrective action. Drawing on theories of moral behavior (Goodin 1985), strategic behavior (Fombrun and Shanley 1990), and corporate social responsibility (Donaldson 1989), I argue that the global pharmaceutical industry, individually and collectively, have a role to play in addressing the ethical issues associated with CMR outsourcing. I suggest that the main actors and stakeholders all have joint and individual responsibility to address the ethical concerns that arise with outsourcing in the industry. Sixth section, the concluding section, presents a summary of the practice and research implications of this article.

This research is limited to ethical and moral issues associated with the outsourcing of CMR to global destinations, rather than on the ethical issues of medical research in general. While the former is limited to the ethical issues in a sponsor–client relationship, the latter focuses on such fundamental ethical issues as profits, pricing, and patient rights as they relate to medical research, drug development, and marketing. These are beyond the scope of this article. The interested reader is referred to Santoro and Gorrie (2005), for a discussion of those and related issues in the pharmaceutical industry. The term "emerging markets" as used here refers to countries that are new destinations for outsourced clinical research. Although most, including top destinations such as India, China, Mexico, Brazil, and South Africa, are emerging economies in common usage, some emerging markets such as Russia and some Eastern European destinations are economically more developed.

Clearly, there are important benefits for the global pharmaceutical firms and sponsors, the two main parties in medical research outsourcing. Pharmaceutical companies benefit from cost-savings and reduced time in getting their drugs to market. Today, global pharmaceutical giants such as Novartis, Astra Zeneca, Eli Lily, and Pfizer continue to outsource medical research globally. Destination countries and their sponsor companies, for their part, benefit economically. For example, estimates are that India earned about $70 million in 2003, with projections of about $200 million by 2007 and $1.5 billion by 2010 (Maiti and Raghavendra 2007).

Despite the attraction, the continued globalization of CMR may be jeopardized if the ethical concerns and issues associated with this business model are not recognized and addressed. Indeed, some critics have already sounded the alarm bells by describing destination countries of medical outsourcing as serving as "guinea pigs" to the world (Shah 2006). Other legitimate fears about the adequacy of the institutional and regulatory environments of destination countries, as well as the capacity of sponsors to protect vulnerable participating populations have been raised (Kuzu et al. 2006). A failure to address the ethical issues associated with CMR outsourcing can distort the promise of this emerging business model.

Our understanding of the issues may depend on unraveling a number of contextual factors. First, it is important to explore the relationship between the actors in CMR, specifically the nature of private governance arrangements they deploy as well as the key features of CMR, including relationships between sponsors and clients. This is important because governance arrangements confer rights and responsibilities regimes on the parties (Williamson 1985). Second, it is important to examine the institutional and regulatory environment facing sponsors as these factors influence and sometimes shape business behavior (Delios and Beamish 1999). Third, examining the adequacy of the global regulatory regimes such as the Helsinki Declaration (an international medical regulatory regime) will be important since most national regulatory regimes are based on such supra-national regimes. Finally, our understanding of how attributions of moral responsibility are made within the context of medical research outsourcing will be crucial to any attempts to understand assignment of responsibility for action. As Driver (2008) notes, the notion of causation is important to moral responsibility since most people think that someone is morally responsible for an event only when that person caused the event (see for example, Naverson 2002).

The global pharmaceutical industry presents an interesting context for exploring these issues for at least two

reasons. First, outsourcing has become a common feature in this industry. Indeed, the new business model for the industry seems to be the rapid globalization of drug research. For example, it is estimated that pharmaceutical outsourcing today is worth about $48 billion. Second, the ethics of medical and clinical research, in general, are well-documented (Santoro and Gorrie 2005).

There are two notable discontinuities in the global pharmaceutical industry. First, is the emergence of a new research model in which clinical research and drug development has shifted from the citadels of academic institutions to commercial outfits, notably, contract research organizations (Bodenheimer 2000). This shift in research from universities to CROs is a result of the fact that CROs combine greater speed, cost savings and efficiency in drug trials, making them a better option for pharmaceutical companies who are focused on speed and cost savings.

A second and related discontinuity, and this is the focus for the present research, is the outsourcing of clinical research to emerging markets. Multinational corporations like Pfizer, Eli Lily, GlaxoSmithKline, Sanofi Aventis and Roche have started clinical studies abroad, with India the preferred destination. Other leading emerging destinations include Indonesia, Thailand, Mexico, Brazil and South Africa (Santiago-Rodriguez 2008) with China angling for a piece of the outsourcing pie (Hepeng 2007).

Motivations and Facilitating Conditions for CMR Outsourcing

Strategic Imperatives for Outsourcing in Global Pharmaceutical Industry

The outsourcing of medical research to emerging markets seems driven by a number of imperatives. First, preliminary reports indicate that pharmaceutical companies are having a hard time recruiting enough patients for drug trials in their home countries. Maiti and Raghavendra (2007) report that on average it takes more than 4,000 patients for the Food and Drug Administration to approve an experimental drug for marketing, and yet fewer patients in the United States are willing to participate in clinical trials. Second, research indicates that governments in Western countries are increasingly tightening their regulations, including imposing more stringent safety and compensation requirements in the face of a dwindling population from which suitable samples can be drawn. Third, is the need for speed in drug development. It is estimated that drug development, a costly and time-consuming process, can take anywhere from 9 to 12 years. Pharmaceutical companies are exploring ways to conduct trials more quickly and inexpensively. Each day's delay in gaining FDA approval of a drug, the manufacturer loses, on average, $1.3 million in potential revenue (Bodenheimer 2000). Fourth, developments in some of the destination countries have made medical research outsourcing more attractive. One top destination, India, for example, brings a fairly well educated pool of researchers as well as a diverse population of more than a billion people who have diseases ranging from tropical infections to degenerative disorders, making them an attractive pool for drug testing (Joseph 2008). The development of institutional infrastructure in India has also provided the impetus for the growth of foreign medical research outsourcing. For example, in January 2005, India adopted new rules that allow pharmaceutical companies to begin clinical trials concurrently with similar trials being conducted abroad, thereby reducing clinical development time (Maiti and Raghavendra 2007). India also became a signatory to intellectual property protection rights in 2005 by amending its Patents Act to bring it into compliance with the World Trade Organization's Trade Related Intellectual Property Rights "TRIPS" agreement (Cekola 2007). China, for its part, may also be transforming into an attractive destination for medical research outsourcing even though a lack of acceptable standards remain a barrier for outsourcing medical research on a wide-scale. The Chinese government has improved the environment for clinical trials by implementing a series of important legislative measures including protecting intellectual property following China's entry into the World Trade Organization (Hepeng 2007). Finally, CROs in destination countries are in a better position to execute drug trials because they clearly have a deeper understanding of local language, culture and norms of their respective countries. These qualities should lead to better relations with investigators and improved trial execution.

The Nature of Clinical Research

Universal principles guide research involving human subjects. Although there are variations in the nature and forms of regulation applied to clinical research on human subjects across the globe, all countries subject clinical research to certain ethical and regulatory norms. Most of these global norms arose out of the post-World War II trials and the Nuremberg Code that emerged out of those trials. The Code consists of ten key principles, among which the most important appears to be that human subjects must give their voluntary consent, must not be coerced in any way, and have the right to withdraw from a study at any time (World Medical Association 1999).

The Declaration of Helsinki, an offshoot of the Nuremberg Code, first published by the World Medical Association in 1964, puts patient safeguard before the

advancement of science. The Declaration affirms the primacy of the concept of informed consent. Helsinki also introduced ethics committees as the primary watchdogs in medical research. Ethics committees go by various names around the world including Institutional Review Boards (or IRBs in the U.S.), Research Ethics Boards (REBs, Canada), Research Ethics Committees (RECs, many Western European countries), Helsinki Committees (Israel), Bioethics Committees (Poland) and Committees for Ethical Protection (CEPs, Brazil). The Helsinki Declaration states that trial protocols should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. The ethics committee is also charged with reviewing the trial on an ongoing basis. The Declaration of Helsinki has been updated several times since its inception. The fifth revision, in October 2000, emphasizes the duty that doctors owe to the participants in medical research. It adds that every patient entered into a study should have access to the best treatment identified by the study after the study is completed.

Ethical Issues in CMR Outsourcing in Emerging Market Environments

Ethical issues associated with outsourced CMR in developed countries are beyond the scope of this article. As mentioned earlier, ethical issues associated with outsourcing CMR to emerging market situations warrant greater attention because of the unique context in which they take place. A recap of the contract research process will be helpful. A pharmaceutical firm outsources its drug trial to a CRO in an emerging market. In turn, these CROs locate researchers and facilities that conduct this research on their behalf. Individual researchers are required to follow the protocols that the client firm gives the CRO. CROs often design trials, monitor them and write manuscripts either by themselves or through commercial manuscript writers. Commercial manuscript writers are individuals or organizations who write manuscripts to be presented for publication against a certain fee without being part of the investigations (Abbas 2007). Local review committees serve as watchdogs ensuring that researchers follow the protocols. In some cases, researchers can apply to the pharmaceutical companies to change the protocols when they deem them onerous and the client firms are free to grant that exemption if they deem it necessary (Fisher 2008).

Violation of ethical rules occurs when contract researchers engage in behavior that violates basic universal ethical norms. In the case of CMR outsourcing, ethical violations can range from a failure to follow established protocols to testing drugs illegally on subjects or failure to safeguard patient rights in any shape or form. Research malfeasance in emerging markets can also include the exploitation of disenfranchised groups (Kuzu et al. 2006). The poor and uneducated can be lured by monetary compensation to participate in a study. In that case, consent, even if given freely, raises ethical questions such as whether such consent was unduly influenced by the prospect of rewards. Other instances of clinical trial misconduct are usually due to insufficient analysis of medical indications, ignoring patient preferences and informed consent especially in situations where subjects may not be educated enough to fully understand what they are getting themselves into (Laughton 2007). Finally, the weaknesses of existing regulatory regimes in emerging markets means that unless individual researchers themselves engage in a certain amount of self-monitoring, the possibility of abuse of the process exists.

The Context of CMR Outsourcing

Nature of Clinical Trial Outsourcing

Ethical concerns in CMR emerge primarily as a result of the stage of the drug development process that is outsourced. According to Hara (2003), drug development goes through several distinct phases. These are: (1) Discovery, which often begins with target identification—the basic research process that involves choosing a biochemical mechanism involved in a disease condition, (2) Product characterization. Early stage pharmacology studies help to characterize the underlying mechanism of action of the compound, (3) Formulation, Delivery, Packaging Development. Drug developers must devise a formulation that ensures the proper drug delivery parameters. (4) Preclinical Toxicology Testing. Preclinical testing analyzes the bioactivity, safety, and efficacy of the formulated drug product, (5) Bioanalytical Testing. Bioanalytical laboratory work supports most of the other activities in the drug development process, (6) Clinical Trials. It is clinical trials that are often outsourced to sponsors. Clinical studies are grouped according to their objectives into three types or phases: (1) Phase I, Clinical Development—Phase I studies are used generally in healthy volunteers to determine things like tolerance; (2) Phase II, Clinical Development—Phase II clinical studies are small-scale trials to evaluate a drug's preliminary efficacy and side-effect profile in 100 to 250 patients; and, (3) Phase III, Clinical Development Studies which are large-scale clinical trials for safety and efficacy in large patient populations.

In the United Sates, the Food and Drug Administration (FDA) review begins with stage 4, the pre-clinical phase

where an application for a new Investigational New Drug application (IND) is submitted. Companies, research institutions, and other organizations that take responsibility for developing a drug must show the FDA results of preclinical testing conducted on laboratory animals and their proposal for human testing. At this stage, the FDA determines whether it is reasonably safe for the company to move forward with testing the drug in humans. According to FDA regulations, clinical trials that involve drug studies in humans can begin only after an IND is reviewed by the FDA and a local institutional review board (Parexel R & D Sourcebook 2001).

It is the middle stages of late preclinical testing, the phase that involves early human testing, that is often contracted to CROs. This stage involves key activities such as the design of the trial protocol with physicians. This phase also involves large-scale phase III clinical trials. The determination of sample size, test parameters, data collection and analysis are all conducted during this phase. Although the clinical phase is still largely process-driven by regulatory and safety issues (Parexel R & D Sourcebook 2001), this is the stage when most of the ethical issues are most likely to arise for two main reasons.

First, contract medical research outsourcing tends to occur at a point where the nature and effectiveness of the monitoring mechanisms are most important. For example, the roles of IRBs are critical at this stage for the protection of subjects. However, the preliminary evidence shows local IRBs in some destination countries seem ill equipped to handle this crucial role (Abbas 2007). According to all international standards, clinical trials must be closely monitored by independent ethical committees or IRBs. Whether this oversight mechanism is effective in emerging market contexts or not is open to question and the existing evidence suggests otherwise. In Mexico for example, there is some evidence that the IRBs may not be as effective as they should be. In some cases, the evidence suggests that there is no IRB at all and when present, there may be conflict of interest between members of the IRB and the principals conducting the investigation (Valdez-Martinez et al. 2006). Researchers have documented other cases of direct unethical trials. For example, Maiti and Raghavendra (2007) found, among other things, that clinical researchers have tested illegal drugs, conducted studies without IRB approval, and sponsors have misrepresented drugs to secure participation by subjects. Evidence shows that in India for example, contrary to both local and FDA regulations, some clinical trials have been conducted without IRB approval. Clearly, these issues are less likely to have arisen during phases that did not involve human subjects.

Another factor that may contribute to unethical behavior is the nature of the business model in CMR and how that translates into the relationship between sponsors and the client. Once awarded the contract, CROs either conduct the research or use individual researchers or physicians to conduct the clinical trials. Those who participate in contract research are given clearly defined protocols by the pharmaceutical companies to follow. Studies indicate that researchers often discover that following the protocols is not always so clear-cut (Fisher 2008). Researchers often think that there is room for them to bend the rules and establish their own clinical guidelines especially when they determine that a protocol is unreasonable. Fisher (2008) notes that deciding how much to bend those rules draws ethics into the equation. Although pharmaceutical companies are known to be flexible about their protocols and would grant exemptions to researchers when asked, most researchers believe that their professional judgments should trump study protocols (Fisher 2008).

It is not only the behavior of researchers in CMR that raises ethical issues. Even more significant is the relationship between the parties is what contract researchers think about who bears responsibility for ethics in CMR. Fisher (2008) found that contract researchers often believe that third parties such as local IRBs, and governments, not they, are responsible for determining the ethics of the clinical trials they conduct. Their argument is that since pharmaceutical firms hand the protocols to them, the responsibility for ethics should rest with them. The point here is not that contract researchers do not take their role to act with care seriously, most probably do. Rather, as Fisher (2008) notes, the issue is that rather than seeing that as their primary ethical obligation, they see it as merely part of the good conduct of study protocols.

Transaction Governance Arrangements in CMR Outsourcing and the Ethics of Responsibility

At some level outsourcing in general, including CMR outsourcing, reflects the classic choices firms face on whether they should perform a specific activity in-house or have it performed outside the hierarchy of the firm (Dulmin and Mininno 2003). How any exchange is governed has implications for the behavior of parties to the transaction, because by definition, governance confers a rights and responsibilities regime on the contracting parties. The available evidence shows that contracts are the main form of governing the relationship between clients and sponsors in CMR (Fisher 2008). This view of exchange governance is consistent with Transaction Cost Economics (Williamson 1985), a theory of exchange governance. Transaction Cost Theory (TCT) suggests that certain exchange relationships are most suitable to contracting. Williamson (1985) argues that three dimensions of a transaction affect the type of governance structure chosen for the transaction: *asset specificity* (an aspect or feature of an asset that makes

it useful for one or few specific purposes), *uncertainty* (the cost associated with the unexpected outcome and asymmetry of information), and, *transaction frequency* (the frequency with which a transactions occurs). As asset specificity and uncertainty increase, the risk of opportunism increases. According to Williamson (1985), asset specificity is the most important determinant of transaction governance.

Contract Medical Research, by its very nature, makes itself amenable to contracting because there is low specificity associated with medical research, including clinical trials. Low specificity means that little information needs to be exchanged between the sponsor and client once the contract has been signed. CMR also has low asset specificity because once the parameters of the contract are defined the sponsor has all it takes to perform the contract as it is possible to bundle all the information as part of the contracting. Although parties to a contract are unable to foresee all exigencies because of bounded rationality, they nonetheless have the capacity to learn and to look ahead, perceive hazards, and factor these back into the contract. In effect, limited but intentional rationality is translated into incomplete but farsighted contracting (Williamson 1981).

Exploring two service characteristics of contracts may shed more light on why certain forms of opportunism may arise in CMR. According to TCT (Williamson 1985), two service-specific characteristics influence sponsor opportunism: asset specificity and service measurability. Service measurability refers to how difficult it is for the contracting organization to measure the outcomes of the service or to monitor the activities required to deliver the service. In the case of CMR, it is easy to measure outcomes. In principle, it should be easy to monitor the activities that are required to deliver the service since those activities can be identified. However, because the client here is removed both physically and contractually from the process, it becomes costly and difficult to monitor the activities that the sponsor undertakes to perform the contract, even when the client wishes to do so. Under this condition, the client is exposed to the risk of unseen sponsor negligence or non-performance. Indeed, agency theory postulates that shirking increases when principals have trouble monitoring the quality of an agent's performance (Meckling and Jensen 1976). Negligence in CMR may pertain to non-adherence to established research protocols that result in the abuse of patients and process, thereby raising ethical issues and the preliminary evidence seems to confirm that contract researchers sometimes alter protocols by themselves (Fisher 2008).

Another important aspect of governance is the issue of legal culpability in case of violations. Contracts allow clients, who so choose, to shift responsibility for violations to sponsors by inserting exculpatory clauses in the agreement. Exculpatory clauses are statutory clauses that shift potential risks from one party to another in a contract (Lawrence 2009). The bundling of responsibilities into contracts also means that the client has no incentive to monitor what the sponsor does as long as they deliver on the provisions of the contract. While it is possible to assign legal responsibility through a contract, knowing who has moral responsibility, when and where it is inherent in a transaction, is a more difficult proposition. For the client, there may be the presumption that because they have no control over what the sponsor does, they are absolved of moral responsibility for any ethical violations. The lack of clarity on moral responsibility inherent in contractual governance may create a certain amount of incongruity between what rights and responsibilities the parties have when it comes to moral aspects of their behavior. In the present case, it may leave sponsors without clear guidelines on moral culpability and may afford client firms a window to side-step legal responsibility for ethical violations by inserting exculpatory causes. Both conditions create ambiguity on moral issues and related research in organizational behavior suggests that a lack of clarity on moral responsibility increases the prospects for unethical behavior (Waters and Bird 1987).

Outsourcing as Cost-Minimizing Choice

Both sponsors and clients in an outsourcing relationship are seeking to create strategic value for their firms. While the client uses outsourcing to economize on transaction costs, the vendor, on the other hand, seeks to maximize profit by minimizing their operating expenses (Jiang et al. 2007). Behaviors that ultimately raise ethical concerns are one outcome of using cost-minimization as a decisive criterion for creating strategic value. It is clear why cost savings is a strategic objective for clients. Current estimates put the cost of developing a new drug and bringing it to market between $800 million and $1.5 billion per drug (Sinha 2004). Like most outsourcing decisions, the prospect of substantial cost minimization and savings is a prime motivation for the outsourcing of contract medical research to emerging, often lower-wage countries. Minimizing clinical trial expenses is important to pharmaceutical companies because clinical trials account for up to 60% of a drug's development cost (Vogel 1999).

Unlike the client, sponsors are driven by the need for profit maximization which they achieve by both lowering their bidding prices as well as cost savings that may arise from economizing on operational costs relating to the execution of the contract (Jiang et al. 2007). Since the client's primary decision criterion for selecting a sponsor is cost savings, sponsors have the incentive to demonstrate that they indeed can offer the lowest cost. This also means

that sponsors may sometimes be compelled to accept contracts at a loss. As van Tulder and Mol (2002) point out, sponsors might have to undercut prices in order to get the contract, to the point that sponsors sometimes make unrealistic bidding promises to win the contract and may be unable to recover their business and operating costs, leading to what Kern, Willcocks and Heck (2002) call the "winner's curse of vendors." Kern, Willcocks and Heck (2002) found from their study that as much as a quarter of outsourcing deals are in the winner's curse mode. From the client's perspective, any contract that governs an outsourcing relationship is often incomplete because of the existence of information asymmetries. While the client is often unable to define exact baselines and the potential for additional costs in the future, the vendor may be in a better position to be able to determine these (Jiang et al. 2007). At any rate, the vendor, as much as the client, has incentives to minimize costs and maximize profits.

The fact that cost minimization is the primary driving force from both the sponsor and client's perspective may open both parties to behaviors that may either raise ethical issues or pressure one or both parties to engage in behaviors that may be ethically questionable. This is especially the case with sponsor (vendor) behavior in emerging countries. In environments with weak regulatory enforcement, the possibility exists that some sponsors may cut corners to save on operating costs. The sponsor may be more knowledgeable about the outsourced product or service than the client may. This makes it unlikely that the client has any idea on the nature of cost-cutting behaviors the sponsor engages in. For example, sponsors have been known to conduct clinical trials in India without undergoing ethical reviews by the Internal Review Boards (Maiti and Raghavendra 2007), a clear violation of the rules, but one that could save the sponsor time and cost. In addition, sponsors have the incentive to offer individual researchers and facilities minimum compensation to increase their payoff. Fisher (2008) reports from his study of contract research in the USA that contract researchers are sometimes driven by cost considerations. Cost minimization makes strategic and economic sense, however, there may be issues when examined from a moral and ethical perspective because of the sort of behaviors it may encourage on the part of actors. Cost-minimizing behavior may raise the possibility of the violations of ethical guidelines, especially where regulatory environments of destination countries are weak.

The Adequacy of Supra-National Institutional Governance Arrangements

The pharmaceutical industry is one of the most regulated industries in the world (Dukes 2005). A question remains whether this widespread regulation is effective in attenuating ethical and moral violations associated with this industry. Looking at the nature of regulations, including provisions for overseas activities in the US, European Union and at the supranational level in the form of the Helsinki Declaration in its original form, and subsequent updates, can give clues to the nature of ethical issues that may emerge as pharmaceutical companies outsource some of their activities abroad, especially to regions that may have less stringent regulations.

In the United States, the FDA provides guidelines for drug testing (the relevant clauses can be found under the FDA guidelines 21 CRF 312.120). Until it recently changed its policy on international drug testing, the FDA guidelines on foreign clinical trials stipulated that foreign clinical trials are acceptable when they provide protection to human subjects. The FDA declared that firms engaged in foreign drug trials should be guided by ethical principles contained in the 1989 version of the Declaration of Helsinki and or the laws and regulations of the country in which the research was conducted. The FDA recognizes the importance of outsourcing in the pharmaceutical industry and has some specific provisions for governing outsourcing relationships. The FDA provides guidelines on how responsibility is to be assigned in clinical trials when contract research is used. Section 312.52 of the FDA Guidelines provides, inter alia, that pharmaceutical companies can use contracts as a means for transferring responsibilities to the CROs. It provides that any or all sponsor obligations may be transferred and that any transfers must be described in writing. It also provides that where pharmaceutical companies transfer any obligations of fulfilling FDA guidelines to the CRO, any such obligation being assumed by the CRO must be described. It notes that the sponsor can transfer all or some of the obligations and where all obligations are transferred, a general statement to that effect is acceptable. Finally, the FDA stipulates that any obligation not covered in a contract shall be deemed not to have been transferred by the client to the sponsor.

In a move that has probably weakened existing governance mechanisms in CMR outsourcing, the FDA decided in 2008 to no longer hold pharmaceutical companies to the standards of the World Medical Association's Helsinki Declaration while conducting human trials citing the fact that even with the Helsinki Declaration in effect, many international drug trials run by American pharmaceutical companies are not reported until after they are conducted, and therefore the FDA was unable to regulate them (Nelson 2008). The revised FDA guidelines require that pharmaceutical companies comply only with local regulations where the trials are conducted. As Nelson (2008) observes, when trials are conducted in a country with little or no

existing health care infrastructure, the "local standard of care" to which the new FDA guidelines refer may not even exist. In a scathing editorial calling on the FDA to rethink its rejection of the Declaration of Helsinki, the scientific journal *Nature,* asserts the FDA risks sending the message that "ethical considerations are expendable when research subjects live half a world away" (Nature 2008, p. 428).

Starting from October 2008, the FDA has replaced the Declaration of Helsinki with new standards it calls *Good Clinical Practice* (GCP), which is modeled on a 1996 document developed by drug regulators and the pharmaceutical representatives from the United States, EU and Japan. The *Nature* editorial notes that although GCP deals with subject protection, it fails as a human rights document, citing its silence on a critical issue such as the use of placebos, an issue on which the Helsinki Declaration is explicit. The Declaration forbids the use of placebos for serious conditions where proven therapies exist. One suspects that this revised policy is well-intentioned. After all, the FDA remains the strongest bulwark against abuse in medical research. However, as the editorial in *Nature* suggests, such an action risks being interpreted as a green light to pharmaceutical companies to underreport their drug trials, leading perhaps to a weakening of the overall regulatory regimes for CRM outsourcing.

The EU, for its part, is reported to be implementing some of the most stringent regulations of the pharmaceutical industry to date (Daemmrich 2003). The guidelines governing drug testing can be found in Directive 2001/20/EC of the European Parliament and the Council of the European Union (based on Council Directive 75/318/EEC of 20 May 1975). Similar provisions for the protection of human subjects and legal consent compliance with the standards of good clinical practice are outlined in the directive. The European Union's (EU) implementation of the Clinical Trial Directive (CTD) into laws, regulations, and administrative provisions is said to represent one of the most demanding changes faced by pharmaceutical companies operating in Europe in the past 30 years. Although the main objective of the EU CTD was to define a more homogenous and consistent regulatory environment that offers maximum protection to participants in clinical trials (an area comprised of some 450 million people), industry experience shows that some old processes have not been decommissioned, but new ones have been added. Most disturbingly, it has been suggested that provisions of the EU CTD are being interpreted inconsistently by the member states (Flavell et al. 2003).

Since both the EU regulations and the initial FDA guidelines and national regulations are based on the Helsinki Declaration, it will be useful to briefly summarize its main provisions. The Declaration of 1964, and its subsequent seven amendments are widely regarded as the cornerstone document of human research ethics. Although not legally binding internationally, the Declaration has become important since it serves as a basis for national regulatory policy in medical research. The Declaration is a statement of the basic principles for ethical medical research. Among other provisions, it stipulates that in pharmaceutical trials, a control group should not be given an ineffective placebo in place of another drug that is known to be effective, as this would leave a sick patient without known effective treatment. The Declaration also requires that participants in any drug trial give informed consent. The updated "Good Clinical Practice" guidelines of the Declaration include protection of human rights as a subject in a clinical trial. It also provides assurance of the safety and efficacy of the newly developed compounds as well as standards on how clinical trials should be conducted and further, it defines the roles and responsibilities of clinical trial sponsors, clinical research investigators, and monitors.

No matter how many updates evolve out of the Declaration, its main weakness is that it is a voluntary guideline and there are no provisions for sanctions. As a self-enforcing regime, it relies on the individual actor's sense of commitment to the Declarations. Self-enforcing regimes are notoriously weak because there are often no mechanisms for enforcing sanctions, even where they are an option (Wortuba 1997). In summary, the weaknesses of supra-national guidelines, some of which form the basis of national guidelines, means that the possibilities for ethical violations in CMR exist. Indeed, the lack of sanctions and reliance on self-enforcement means that the integrity and effectiveness of the supra national guidelines are questionable.

Local Contextual Factors

It is important to consider the local and institutional circumstances when clinical trials are conducted internationally and the preliminary evidence suggests that the institutional and cultural context of emerging markets presents ethical challenges (Jonsen et al. 1992). As the premier destination for contract research, India's institutional context is revealing and examining the case of India may illustrate some of these key issues associated with CMR outsourcing in emerging countries. The problem, for the most part, may not be a lack of policy. Rather, the weak link appears to be implementation and enforcement. What is interesting is that there are close similarities between the regulation of clinical trials in both the US and India. The Indian regulations for clinical trials are found in Schedule Y of the Indian Drugs and Cosmetics Rules (Cekola 2007). As Cekola (2007) points out, both India and the US, require governmental approval before a clinical trial starts. There

are third party reviewers: the IRB in the United States and its equivalent in India, institutional ethics committees (IEC). Unlike the US, India relies on IECs, rather than the government, to exercise oversight over medical research. In India, the ethics committees are the sole parties that review the detailed protocols and assess the risk of an investigational trial on test patients, while in the US, both the FDA and the IRBs assess the protocols and risks. India, like US, has regulations for protecting human test subjects. Informed consent and voluntary participation are all clearly specified in Schedule Y of the Indian Drugs and Cosmetic Rules (Cekola 2007). Despite the existence of these internationally accepted rules and regulations, their implementation may be hampered by the unique context of emerging countries for a number of reasons.

First, it is well known that the pressure to attract foreign investment means that local enforcement of laws and regulations may be lax. Given that emerging and developing countries are motivated to encourage their local firms to seek business in clinical research and trials, there may be instances where even existing laws and regulations may not be rigorously enforced. At other times, economic pressures may lead to the dilution of regulations. For example, Singh (2007) reported that an amendment proposed in 2007 by the technical advisory committee of India's Health Ministry would further allow drug companies to test their products widely on patients in India, even before they are proven safe in the home countries of clients.

Second, because the drug testing and research industry may just be emerging in these countries, it is likely that legislation to control the industry lags behind developments in the industry. Third, because enforcement requires the availability of trained personnel, and these countries often suffer from shortages of manpower, it is less likely that violations will be quickly caught and addressed. Nundy and Gulhati (2005, p. 1633), report that the Drugs Controller General of India (DCGI), the equivalent of the FDA in the US, is understaffed and lacks the expertise to evaluate protocols. The authors report that as of 2005, the technical staff consisted of three pharmacists and not a single doctor, making it necessary for CROs to make repeated follow ups, including making personal visits to the DCGI to push their applications for trial forward. The authors also provide data in their research, which shows that despite India's advances in medicine fewer than 200 investigators have been trained in good clinical practice.

Finally, high poverty and low educational levels mean that regulations on key areas such as informed consent and voluntary participation may be overridden by the desire for compensation from participating in drug trials even if the protocols are not rigorously followed, as they should be. When subjects are poor especially, monetary inducements can be used to influence them (Laughton 2007). Thus, both strong institutional environments made up of regulatory provisions and mechanisms for enforcement, as well as a well-educated citizenry capable and willing to ask critical questions before volunteering as subjects for drug trials will reduce the environment for ethical violations. Unfortunately, these do not appear to be the case presently in some of the largest destination countries for CMR.

Stakeholders and Moral Responsibility

Assigning Responsibility

Our earlier discussion established that clients can legally bundle and transfer responsibility to sponsor organizations. Sponsor organizations, in turn, can transfer responsibility to individual facilities and researchers who carry out the basic work. Discussion also was that contract medical researchers might not always accept responsibility for their behavior. Indeed, Fisher (2008, p. 2500) quotes a US researcher who noted that contract researchers cannot be blamed for potentially endangering subjects when the responsibility comes down not only to the pharmaceutical companies developing the products, but also to the US government setting the rules for those companies to follow. Of course, not all contract researchers may share this view, but this coming from one of them is telling. The issue then becomes how we ascribe responsibility and blame when harm is caused to research subjects in the performance of outsourced CMR.

Prior research has shown it is easier to assign blame when there is only one actor involved because it is easier to link cause and effect (Alicke 1992), but that is hardly ever the case in practice. It is no surprise that the question of assigning moral responsibility has often been a subject of debate in moral psychology (see for example, Knobe and Fraser 2008; Deigh 2008 for some opposing view). At the heart of that debate is whether someone should be morally responsible for an act that they did not directly cause. This issue is of paramount importance in this discussion since pharmaceutical firms as clients are far removed from the performance of the outsourced clinical studies. Similarly, it may be difficult, to hold any stakeholders not directly linked to causing any harm by their acts of omission or commission responsible for ethical malfeasance in CMR.

Two general views emerge on this debate: those who support the idea that someone is morally responsible for something only if their actions directly caused harm and those who argue otherwise. First is the view that someone is morally responsible for an event only when that person has caused the event. Thus, we can argue, based on this principle, that client firms cannot be held responsible because they are not in a position to cause any harm to

research subjects. This is the so-called entailment claim that moral responsibility entails causal responsibility (MC). Driver (2008) reformulates moral claim (MC) as follows:

> MC If an agent A is morally responsible for event *e*, then, A performed an action or omission that caused *e*.

There are those who oppose this MC position. Critics of the entailment claim cite instances in which causation need not be present for harm to occur. For example, Sosa (1993) argues that acts of omission have no direct causal effect, but can nonetheless lead to harm. Similarly, Leslie (1991) argues that we can hold someone responsible for outcomes even if they did not directly cause the outcome but that would not have occurred but for their actions, what he terms "quasi-causation." For example, an individual, A, can be said to be morally responsible (as per quasi-causation rule) if he/she forgets to lock the doors to the apartment they share with B, the house is burglarized, and B is assaulted during the break-in resulting into serious physical injuries. A's responsibility arises because a failure to lock the door was a contributory factor in the robbery. In other cases as Deigh (2008) points out, sometimes being part of a causal chain does not necessarily make one morally responsible, as is the case of a postal worker who unknowingly delivers a bomb that kills someone. Even though he/she is part of the causal chain leading up to the death, we cannot hold him/her morally responsible. These are valid counterexamples to the MC claim.

Interestingly, proponents of the MC claim accept that not all cases of causal responsibility for an event makes the agent morally responsible but state, instead, that when someone is morally responsible, they must have been the cause of the event (Driver 2008). We can navigate this philosophical minefield by introducing an important qualifier, one that is probably more reflective of how average people assign moral responsibility. As Driver (2008) notes, it is quite true that when people pick out *the* cause of an event among a nest of causal factors, they often rely on normative, pragmatic and contextual considerations. For example, in using commonsense ascriptions of causation, people are likely to decide who they think is blameworthy or responsible and then assign causation (Hart and Honoré 1959).

Based on the above analysis, we can make some preliminary allocation of responsibility for any ethical violations associated with CMR. In the case of individual researchers and research facilities, the application of the MC principle is straightforward. The MC claim leads one to assign blame when either actor violates any ethical guidelines associated with medical research. Second, client firms, host governments and CROs can nonetheless be subject to blame and responsibility even though they may not have directly caused any harm. Following Leslie's notion of "quasi-causation", we can assign blame to clients for any harm to research subjects, if and when they happen in the course of outsourced medical research. The logic here of course is that, such harm would not have happened but for the fact that CMR is outsourced in the first place. The same logic can be applied to host governments for their failures in either developing or enforcing laws to police medical research in their countries. At a pragmatic level, and this is what is more likely to inform our intuitions, one is probably more likely to assign blame to the more visible and powerful actors such as global pharmaceutical firms and governments even if they are not directly the cause of an event, rather than to individual researchers who may have had a direct role in causing the harm. Indeed, as Clark (2009) observed, problems with trials sponsored by multinational companies are likely to receive more press attention, even though ethical and quality violations often occur in trials initiated by local investigators. For example, it is reported that Indian doctors initiated several unauthorized trials of cancer, contraceptive and fertility agents, none of which involved participation by Western sponsors (Nundy and Gulhati 2005). Often, such incidences receive less publicity than problems associated with global companies. Based on these preliminary claims, it is clear that all the stakeholders may have to assume a certain degree of moral responsibility and blame in the event of ethical violations in contract research, with the larger, more visible pharmaceutical firms likely assuming a larger portion of the blame when violations become known.

Imperatives for Action

Moral Imperatives

Protecting the vulnerable is a principle that is upheld by most, if not all, ethical traditions. One moral theory in particular, Goodin's (1985) moral theory and his principle of protecting the vulnerable, seems appropriate as a framework for understanding the responsibilities of actors in CMR to protect those who may suffer from any deleterious effects of their activities, and I borrow from his work to elucidate this section of the article.

Arguing for the moral need to protect the vulnerable in all situations, Goodin puts forth two principles of responsibility: individual and group responsibility. Goodin asserts that a moral agent is responsible for the consideration of the interests of all those who will be affected by his/her actions. Goodin qualifies this general responsibility by observing that the demands of this principle are mitigated by such factors as the (1) capacity of the agent to perform, (2) coherence of the demand of the vulnerable with the

other obligations of the agent, and (3) the degree of awareness of the vulnerability present or what is reasonably expected of the agent. More formally stated, Goodin's *First Principle of Individual Responsibility* states that if A's interests are vulnerable to B's actions and choices, B has a special responsibility to protect A's interests and the strength of this responsibility depends strictly upon the degree to which B can affect A's interests.

Goodin goes on to suggest that this moral claim does not mean that moral agents have some universal call to protect everyone from everything. People are limited by what they know their abilities allow them to provide, the remedy a claimant requires, and the agent's capacity to do so. Also, an agent must know the claim exists in the first place and whether a more pressing moral claim trumps a current one. Goodin develops his first principle into a principle of group responsibility, in which each member has the responsibility as far as she/he is able to (1) ensure the organization of the group to respond to those vulnerable to its actions, and, (2) discharge their own allocated responsibilities. Goodin (1985, pp. 134–136) decomposes moral responsibilities into what he calls disjunctive and conjunctive responsibilities. According to Goodin, moral agents have disjunctive responsibilities when one particular person within a group is in the best situation to help the vulnerable. While the person best placed is required to render assistance, other people's responsibilities are not erased, but merely reformed. In other words, if others within the group determine that the assistance of others are required to help the vulnerable, then those individuals also have moral responsibility to help. In contrast, conjunctive responsibilities occur when a vulnerable person can best be helped when a group of people act cooperatively. This leads Goodin to his principle of group responsibility: If A's interests are vulnerable to the actions and choices of a group of individuals, either disjunctively or conjunctively, then that group has a special responsibility to (a) organize (formally or informally) and (b) implement a scheme for the coordinated action by members of the group such that A's interests will be protected as well as they can be by that group, consistent with the group's other responsibilities. Goodin's group responsibility principle holds everyone accountable, whether one has a disjunctive or conjunctive responsibility or not, leading to his second principle for individuals as members of the group: If B is a member of a group that is responsible, under the principle of group responsibility, for protecting A's interests, then B has a special responsibility: (a) to see to it, so far as he is able, that the group organizes a collective scheme of action such that it protects A's interests as well as it can, consistently with the group's other responsibilities, and, (b) to discharge fully and effectively the responsibilities allocated to him under any such scheme that might be organized, in so far as doing so is consistent with his other moral responsibilities, provided the scheme protects A's interests better than none at all (Goodin 1985, p. 139). Despite the fact that a lack of information and resources may always mitigate the responsibility of both individuals in a group as well as the group, Goodin's principles place substantial responsibility on each individual agent, even in group situations.

Goodin's theory of collective responsibility has support in Feinberg's (1970) taxonomy of collective responsibility in which he notes that a group can be held liable even though not all of their members are at fault and that a group can be held collectively responsible through the fault, contributory or noncontributory, of each other. It is important to note that not all moral traditions accept the notion of collective moral responsibility albeit there are those who argue, consistent with Western ideals of individual moral responsibility, that individualism is the only rational meta-theory for collective responsibility (see for example, Naverson 2002; Thompson 1987) and so only those directly involved in an act are responsible.

Goodin (1985, p. 127) provides another important concept on moral responsibility: he distinguishes between what he calls causal and task responsibility to show that causal histories should not necessarily play a part in determining the responsibilities involved in any given situation. While one acquires task responsibility simply by being in a position to affect a situation, one acquires causal responsibility by participation in the antecedent conditions leading to the event. Goodin adds an important restriction to his "dire need" clause, which states that one's moral obligations to help others, really begins when the other is truly unable to help him/herself and is therefore in "dire need" of aid. Pierlott (2004, p. 587) observes that while extreme situations may demonstrate vulnerability and dire need, it may be that it is not only extreme situations that invoke moral obligation.

Goodin's principles may provide a framework for understanding the moral obligations of sponsors and clients in CMR to protect the vulnerable. Both Goodin's individual and group responsibility principles assign responsibility to both sponsor and clients. His moral principle for protecting the vulnerable suggests that both sponsors and clients have a responsibility to protect those who they deal with in the discharge of their contracts. While the first principle and the notion of causal responsibility confer important responsibilities on sponsors since they are in direct contact with research subjects, the concept of task responsibility suggests that contracts may not abrogate the moral responsibility of client firms but merely reform them. Indeed, while the client has no direct causal responsibility, it still has a moral obligation (disjunctive responsibility) to ensure that subjects are treated well and that the sponsor protects the vulnerable. Indeed, the limiting clauses of self-

interest hardly free the client from moral responsibility in CMR outsourcing. In fact, subjects in most developing countries may have a "dire need" to be protected and Goodin's dire need clause may be especially applicable to research subjects in developing countries. Contextual factors such as low educational levels, weak institutional protection, and poverty all mean that such individuals are in the most vulnerable situations, unable to help themselves, thus meeting Goodin's dire need criterion. From a moral argument perspective then, both clients and sponsors have individual and group responsibility to act with due care in CMR outsourcing.

Strategic Imperatives: Reputational Effects

At least two strategic reasons exist as to why client companies need to pay attention to some of the ethical issues that arise in CMR outsourcing: the loss of reputation when abuse of medical research is associated with their name and the limits of contracts as a tool for legal protection. The first strategic imperative relates to the possibility of large pharmaceutical clients losing their reputations when a sponsor or their agent is found to have acted unethically while conducting clinical research on their behalf. Ironically, this imperative may be based on the strategic self-interest of the firm. Pharmaceutical companies stand to lose their reputation when sponsors involved in trials on their behalf do something wrong or commit an unethical act. Although the contracts governing outsourcing entail arms-length relationships, society is less likely to consider that when they judge the pharmaceutical company whose sponsor acts unethically.

As Dukes (2005) observes, the pharmaceutical industry is a potent force for good in the community, yet its behavior is frequently questioned and its reputation not exactly stellar. Incidentally, global managers have acknowledged that reputation is important. Reputation, defined as the public's affective evaluation of a firm's name (Fombrun and Shanley 1990), is an important strategic asset that affects, among others, a firms' ability to obtain new clients as well as retain existing ones (Wilson and Grimlund 1990). Once damaged, reputation takes time to repair (Hale et al. 2005). Rhee and Valdez (2009) suggest that third parties may play an important role in reputation building and repair especially because the public may not necessarily be aware of a firm's reputation damaging events. In the case of pharmaceutical firms, watchdog agencies such as the FDA, local NGOs and press as well as the global media may be especially important in outing ethical violations by sponsors. Rhee and Valdez (2009) note that when prestigious media airs some violation, the visibility that comes with it may be rather damaging to the firm. In the case of the pharmaceutical industry, such bad publicity has already happened to some firms. Pfizer, a global pharmaceutical giant, has been at the receiving end of negative publicity lately for its drug testing in Nigeria (Stephens 2000). Global pharmaceutical firms therefore have a strategic reason to ensure that those involved in contract research on their behalf conduct themselves ethically.

The Limits of Contracts

The second and related reason for clients to be mindful of the actions of their sponsors relates to the very limits of the law. Legal theorists suggest that the courts are often hesitant when it comes to enforcing exculpatory clauses. Indeed, in the US for example, the FDA regulations allow clients to transfer risks to CROs. However, the real issue here is whether such clauses are enforceable, especially in some destination countries. Even in the US, there is some agreement amongst legal scholars that the courts are careful in determining when to enforce these clauses especially when the substance of the contract is medical (Lawrence 2009). A detailed review of legal frameworks in destination countries is beyond the scope of this article. However, the experience of China can serve as one indicator that client companies should be circumspect about relying too much on legal protection in the form of exculpatory clauses in CMR. Lewis (2008), discussing China's Contract Law (Contract Law, Article 53.1), observes that the enforceability of exculpatory clauses seeking to exempt a party from liability resulting from personal injury or death are unforceable, regardless of how such injuries are caused. Lewis' analysis of China's Contract Law suggests that those writing exculpatory clauses into contracts in China need to be cautious about their enforceability. Speculation suggests that in countries with less-developed institutional frameworks, the reliance on exculpatory clauses in medical research contracts may not always offer the protection they are intended to offer. Again, global pharmaceutical companies should not put much faith in legal protection, but instead be ready and willing to engage in extra-contractual behaviors that enhance the capacity of their agents to act with due care especially in emerging markets. One implication here is that global pharmaceutical firms need to be active participants in arrangements that promote ethical behavior in outsourced contract research.

Guidelines for Action

Modifying/Redesigning Governance

CMR governance may need to evolve from purely contract-based, to relational, trust-based forms or a hybrid of

both. Contract-based governance makes it possible for parties to have an arms-length relationship. More importantly, the low asset specificity associated with clinical research offers no incentives for the parties to develop any long-term relational assets. However, a more nuanced understanding of the relationship between sponsors and clients in outsourcing in the global pharmaceutical industry reveals that both parties may actually gain by building a closer relationship, as is often the case in partnerships. At some level, client firms are outsourcing a critical component of their business activities in which unethical behavior by sponsors has economic implications for clients if the violations get into the public domain.

Developing a close working relationship based on norms of cooperation and relationship building with sponsors may reduce the possibilities for opportunistic behavior and build trust between the parties (Heide and John 1992). Relational norms are shared values and expectations about appropriate behavior by parties to an exchange. The presence of relational norms facilitates information exchange between exchange partners, promotes communication, and allows for adaptations to unforeseen developments (Heide and John 1992). The development of a close working relationship should help the building of goodwill between the parties. As Heide and John (1992, p. 34) note, "relational exchange norms are based on the expectation of mutuality of interest, essentially prescribing stewardship behavior, and are designed to enhance the well-being of the relationship as a whole." Most importantly, trust creates a moral duty and a sense of responsibility between the parties. As Treviño and Brown (2004) observed, a sense of personal responsibility is a necessary prerequisite for moral behavior; a belief that one's action may cause direct harm to any one or an exchange partner makes it less likely that an individual would be disconnected from their actions. Sponsor firms or their agents who feel a personal responsibility to their partner firms to act with due care are less likely to act unethically. Also, close relationships will ensure that client firms will be aware of the challenges facing sponsors in developing country contexts. However, the sort of arms-length relationships that contracts encourage may not be as conducive to building relational assets and modifying existing governance structures to include non-contractual ones could prove useful in the end.

Industry-Level Action: Need for an Industry Regime

Goodin's (1985) principle of group responsibility suggests that collective action may be required to address some ethical issues associated with outsourcing. While it may be possible for individual firms involved in CMR to design their own responses to ethical issues, the problems associated with a strategy that has come to be so closely associated with the pharmaceutical industry as a whole may best be addressed through collective action and strategizing. Collective action involves group actions intended to further the interests of members (Olson 1965). Collective action sometimes emerges when participants share a common understanding of particular issues. In the case of medical outsourcing, collective industry standards that translate into industry-wide guidelines for behavior in this area will be helpful for at least two reasons.

First, it will signify to other stakeholders that global pharmaceutical firms have assumed ownership of the problems associated with one of their core business models. Second, it will ensure that some guidelines exist across the industry for actors. Examples of such industry regimes include Responsible Care, a voluntary initiative of the global chemical industry (ICCA, 2000). The industry can use existing standards in their home countries as a guide and some calls have already been made for exporting ethical standards abroad (Shapiro and Meslin 2001). Of course, there are challenges to collective action, especially those that are voluntary and self-regulating. Olson (1965) observes that even if all of the individuals in a large group are rational and self-interested, and would gain if, as a group, they acted to achieve their common interest or objectives, they will still not voluntarily act to achieve that common or group interest. Amongst the vexing problems that can plague industry regimes are the possibilities of free riding, where some members of the group do nothing but reap the benefits (Ashby et al. 2004). Enforcement is also a problem (Detomasi 2007). Some of these problems can be overcome by developing narrow but clear guidelines for members. Individual firms must also demonstrate a commitment to the collective rules by developing internal programs that are consistent with the collective rules. Although often problematic, the development of effective sanctioning mechanisms will be important (Detomasi 2007). Industry actors can set up formal structures for monitoring member behavior. In the end, it may be in the long-term interest of the pharmaceutical industry to act on some of these issues, as failure to engage in self or other-monitoring will only expose the industry to intervention by governments.

Institutional Capacity Building as Corporate Social Responsibility

Client companies can do well to help destination countries upgrade their institutional infrastructure relating to clinical testing and medical research. This will be in their strategic interest and serve as part of their corporate social responsibility (Donaldson 1989). Social responsibility, a form of voluntary corporate initiative, whether viewed as a form of corporate philanthropy or risk management, can have a

positive impact on firms. In the case of CMR in emerging nations, social investment in developing the institutional infrastructure for CMR should have a positive effect on performance.

The disparities that exist between developing and developed countries are reflected not so much in the capabilities of sponsoring firms in developing countries, but in the inadequacies of the institutional infrastructures that govern their work. While CROs and medical researchers in developing nations may have the scientific and intellectual capital capabilities required to execute the research contracts, their weak institutional environments increase the chances of ethical violations. It may be in the long term strategic interest of the big pharmaceutical firms engaged in global outsourcing to help developing countries build and strengthen their institutional infrastructure for medical research and clinical trials. The sharing of knowledge, resources and capacity building will go a long way in reducing the very conditions that may lead to ethical violations. In the long run, the payoffs from such an investment could be substantial and there is some evidence that some of this is already happening. For example, Pfizer India Ltd. is reported to have helped in the establishment of the Academia of Clinical Excellence (ACE), a collection of several institutes dedicated to the study of clinical research and data management. Both India and Mexico have taken important steps to strengthen their institutional capacities in this area and global pharmaceutical firms can play a critical role in this sort of capacity building (Santiago-Rodriguez 2008). Pfizer is also reported to have conducted more than 40 good clinical practice workshops and has trained more than 2000 investigators in India (Maiti & Raghavendra 2007). These are important first steps that require sustained commitment on the part of the global pharmaceutical industry.

Conclusions

Contract Medical Research outsourcing has become an important business model in the global pharmaceutical industry. This means that it is in the strategic interest of all actors associated with CMR to reduce incidences of ethical malfeasance. Without a doubt, a vast majority of client and sponsor firms act ethically; it is in their interests to do so. However, since we are dealing with human subjects, there can, and should not be, any margin for error. This article discussed some structural and behavioral features of CMR and shown how these may give rise to ethical concerns. Using moral behavior and strategic theories, this article suggested that sponsors and clients have both individual and collective responsibilities for ensuring that the ethical and moral issues associated with CMR are addressed. There are important implications of this article for practice and research.

Implications for Practice

First, governments in destination countries need to take into account the unique cultural, social and economic context of their individual countries as they develop regulations for medical research. The Helsinki Declaration and its subsequent updates provide a baseline for what is universally acceptable. For example, informed consent, avoidance of undue influence and patient safeguards are universal norms that ought to be respected. That notwithstanding, it would probably be prudent, and more realistic, if its provisions serve as guidelines, rather than de facto rules since contextual factors may warrant modifications of some rules. For example, the nature and composition of review committees can be modified to reflect the availability or otherwise of qualified personnel. In the end however, it is important that subjects are protected in contract medical research.

Second, governments in destination countries need to develop their institutional capacity for enforcing the laws pertaining to medical research. Enforcement should serve as deterrence to those who may flout established regulations on ethical behavior in medical research. For their part, individual researchers need to have moral clarity and commitment to act with diligence and care as they execute their medical research contracts. In the end, they are the people in the best position for ensuring that subjects suffer no harm.

Third, pharmaceutical companies can use the services of clinical research associates (CRAs) to monitor clinical trials. Often CRAs work directly with the sponsor company of a clinical trial, as an independent freelancer or for a CRO. A clinical research associate ensures compliance with the clinical trial protocol, checks clinical site activities, makes on-site visits, reviews Case Report Forms (CRFs) and communicates with clinical research investigators. Using an independent person as a check on behavior can help reduce abuses of the process.

Finally, sustained dialogue and collaboration among all the stakeholders associated with CMR in emerging markets will go a long way in the design of proactive policies for addressing ethical issues that arise. According to Gray (1989), collaborative approaches to problem solving are best suited when stakeholders are interdependent and when a unilateral effort to deal with the problem typically produces less than optimal results. Lessons from previous experiences in multi-sector collaboration can prove useful (Lawrence and Hardy 1999; Faerman et al. 2001). Stakeholders associated with global CMR outsourcing can set up a facilitative, intermediary organization for accumulating

and sharing knowledge and best practice. The emergence of learning communities will further help the process of collective learning and knowledge sharing.

Implications for Research

There are some research issues worthy of our immediate attention. So far, research on outsourcing has focused mainly on the economic benefits of the practice. In the case of medical research, ethical issues are also an inherent part of the process. It is therefore important that research begins to examine what the ethical issues are and the appropriate remedies that can be put in place to further strengthen this business model. One important area for further research is the question of how moral responsibility is assigned in CMR. As our discussion has shown, there appears to be a clear disconnect in some cases between contract researchers and their clients when it comes to who should assume responsibility when things go wrong. This ambiguity can prove dysfunctional because knowing who is responsible encourages actors to be careful about how they conduct themselves. Our understanding of this critical issue may be rather rudimentary and additional work is urgently required on this topic. To this end, existing research in moral psychology may prove useful.

Second, there is a need for comparative studies of developing and developed country contexts to determine whether the challenges associated with CMR outsourcing are unique, even if magnified in emerging market country contexts. Third, it should be interesting to determine which of the factors discussed are most relevant to global pharmaceutical firms: moral, strategic or social responsibility as the primary reason why firms would go beyond contracts and face the obvious added costs of ensuring that ethical behavior is taken seriously in CMR.

Finally, it will be helpful to know the extent to which contract researchers in developing countries believe they should assume responsibility when issues of ethical misconduct arise in the course of executing their contracts. Fisher's (2008) study in the United States raises an interesting possibility that those directly involved in conducting the clinical trials may actually externalize responsibility for their behavior. It will be interesting to know where they assign that responsibility. Such knowledge can prove useful in developing educational programs targeted to actors associated with CMR outsourcing in destination countries.

Emerging markets will continue to offer global pharmaceutical companies an attractive destination for medical research outsourcing. As homes to sponsoring firms, these countries can similarly benefit from the learning and capacity building that accompanies such economic activity. In the end, however, this symbiosis can only be sustained if the ethical and moral dimensions of the business model receive the attention they warrant. The fact is cost saving and ethical behavior need not be mutually exclusive. To the contrary, well-managed, they can complement each other.

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