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The truth about the truth: What matters when privacy and anonymity can no longer be promised to those who participate in clinical trial research?

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Abstract

The ramifications of including genetic components in the clinical studies conducted in non-academic settings create unique ethical challenges. We used a qualitative research design consisting of semi-structured interviews that took place between October 2010 and September 2012. The sample consisted of 80 participants − 38 physicians and 42 coordinators − who worked across a number of different settings, including clinics, private practices, small hospitals, free standing research centers, and blended hospital-institutes in both rural and urban communities in 13 states across the United States. The respondents primarily conducted industry sponsored trials and recruited their own patients as research participants. A majority of the respondents (65%) reported that most of the studies they conducted included an additional genetics component, and so participants were asked to donate specimens for genomics or biobanking. While genomics association studies were perceived as being of benefit, awareness of ethical implications associated with such studies was limited. The rapid advances in genetic technologies make it hard for clinicians

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and coordinators to help patients make informed decisions about participating in clinical research, and underscore the need to ensure that the regulations governing research on human subjects keep pace with the social and technological changes. It seems essential to discern legitimate ethical concerns and find ways to convey what is going on, what is possible and what might not be possible in terms of protecting privacy, anonymity, and confidentiality.

Keywords
biobanking, clinical trials, genetics, genomics, human subject protection, research ethics

Introduction

In the United States, the federal regulations known as the Common Rule codify the ethical guidelines that underlie research on human subjects. These regulations, first published in 1991, reflect classic distinctions between research and clinical care. In research, the investigator's first loyalty is to the research and its scientific integrity. In clinical care the focus of loyalty is on the individual patient. Among other requirements, the core principles of the Common Rule require that all risks and benefits of trial participation be disclosed in a process that assures a fully informed and voluntary trial participant. These informed consent principles also stipulate that assurances of privacy and confidentiality are in place for those who enroll as research subjects (US Department of Health and Human Services, 1991).

A growing body of research suggests, however, that researchers are doing a poor job educating research subjects about essential aspects of the studies in which they are asked to enroll (Appelbaum, 2010; Iltis, 2006; Morreim, 2009; Sand et al., 2010). Consent forms have grown in length and complexity and often serve more as a legal document that protects the institutions or companies than a document designed to protect and inform the human subjects (Resnik, 2009). Some research suggests that trial participants, regardless of education level or background, show little understanding of any of the key information contained in the informed consent form (Cook and Hoas, 2011). Moreover, subjects seem to overestimate benefits and underestimate risks. In part, this strategy may be based on the belief that their physician or nurse would not suggest enrollment in a study if participation came with too high a risk or was not in the patient's best interests (Cook and Hoas, 2011, 2013a, 2013b).

Dramatic changes in the clinical research setting may further complicate efforts to uphold the tenets of the Common Rule. When the regulations were initially published, the vast majority of biomedical research, including clinical trial research, was conducted in academic settings by highly trained researchers (Chen et al., 2003; Klein and Fleischman, 2002; Snyder and Mueller, 2008). Federal

dollars supported the bulk of this research. Over the past few decades, however, the conduct of clinical trials has undergone notable changes in terms of where they are conducted, who conducts them, and who sponsors them. Today, most clinical research is conducted in non-academic settings by contracted physicians and their staff in private physicians' offices, hospitals, institutes, and clinics (Fisher, 2007a, 2007b; Fisher and Kalbaugh, 2012; Shuchman, 2007). Even very rural settings are engaged in the clinical research enterprise. Most of the clinical research is sponsored by pharmaceutical companies and many studies are designed to fulfill commercial purposes such as extending patents or obtaining a market share. The oversight of the trials often lies with central or independent Institutional Review Boards (IRBs) rather than, as in the past, with a locally sponsored IRB (Wechsler, 2007).

Finally, it may be difficult for researchers to convey key information to prospective subjects because, as a growing body of scholarship notes, the classic distinctions between research and treatment are easily blurred (Appelbaum et al., 2004; Chen et al., 2003; Schwartz and Appelbaum, 2008). Such blurring might be particularly prevalent in non-academic research settings where clinicians serve as both researcher and treating physician, and the patient becomes the research participant. Indeed, the patient electronic records become a primary source for identifying trial participants (Cook and Hoas, 2013a). The physician's ongoing relationship with the patient facilitates enrollment and research participation is often viewed, by both the clinician and the patient, as the means of providing optimal clinical care (Cook and Hoas, 2013a).

Conveying what it means to participate in research trials may become particularly problematic when studies include genetic components. This is a pressing issue given the increasing numbers of clinical trials that now include a genetic component (National Human Genome Research Institute, 2013). In order to accurately convey information about risks and benefits, clinician/researchers need to understand the scope and implications of including genetic samples in studies. They need to have some understanding of the ethical challenges that accompany data sharing and biobanking. They also need to understand how genomic technologies may challenge traditional notions of how to protect and respect those who provide samples.

The article explores the ethical ramifications that can develop when including genetic components into the clinical studies conducted in non-academic settings. The data for this exploration are part of a larger data set assembled for a study that explored how clinical investigators and research coordinators protect human subjects and ensure research integrity when conducting clinical research in non-academic settings. The study was funded by the National Institutes of Health/National Human Genome Institute and was approved by The University of Montana Institutional Review Board.

Background

Currently clinical trials are routinely designed to include a genetic component or association study for which the participants are asked to donate specimens for biobanking. Biobanks are designed for prospective epidemiological research that combines the long term storage of biological samples with databases of DNA sequences derived from those samples, health records, and/or genealogical or lifestyle information on volunteers or patients. It is expected that over time such biobanks will help inform understanding of the causes and pathways of human disease and will result in the development of new drug treatments that may even be individualized.

When genetic components are added to trials, however, many of the established concepts of research ethics are stretched to their limits, and issues of privacy, confidentiality, and consent for research need re-examination (Karp et al., 2008; Lunshof et al., 2008). Unlike clinical research, in which the risks primarily involve physical harm, the risks in biobank research are principally those associated with a loss of privacy and anonymity (Murphy et al., 2009). Indeed, some authors argue that surprisingly small amounts of genomic sequence data are identifiable. In addition, the practice of combining databases may make it possible for investigators to identify individuals, families, and groups (Hayden, 2012; Karp et al., 2008; Malin et al., 2011). In a recent article in *Science*, the authors showed that within hours it was possible to reveal a person's identity by combining information from various publicly available databases and some clever detective work (Bohannon, 2013). The authors of that article caution that in order to avoid losing public trust over these issues, there is a need to revise the way in which the public is informed about the impossibility of ensuring complete anonymity. Authors caution that these issues will become more pressing in the future as genomic technology and information are used outside of research healthcare settings (Rodriguez et al., 2013). Thus, as research migrates into new settings and reaches new stakeholders, it is critical to develop protocols that accommodate the challenges that emerge within an evolving research environment.

Study description

Sample description We employed a qualitative research design consisting of semi-structured interviews that took place between October 2010 and September 2012. We used a two-pronged approach to identify study subjects. First, through the US national registry of clinical trials we identified communities in which trials were conducted and contacted potential research clinicians and coordinators for our study. Particular efforts were undertaken to identify communities that were

non-metropolitan and so ranged in size from 2500 to 50,000 persons. Once contacts were established and interviews secured, we used the snowball technique to identify additional study subjects (Bogdan and Biklen, 2006; Creswell, 1998; Johnson, 2005; Morgan and Krueger, 1997; Strauss and Corbin, 1998). This resulted in a sample consisting of 80 participants − 38 physicians and 42 coordinators − who worked across a number of different settings including clinics, private practices, small hospitals, free standing research centers, and blended hospital-institutes in both rural and urban communities in 13 states across the US.

Data collection The investigators developed a semi-structured instrument that employed a set of core questions while also allowing for the exploration of unanticipated or emerging issues. The clinicians and coordinators were asked to describe their educational background as well as their training in research methodology and ethics, motivations for conducting research, areas of research, and awareness and management of challenging ethical issues. A subset of questions was asked about whether studies included genetics components and, if so, to what extent, how such studies were managed and how they were perceived. The hour-long interviews were conducted by phone, recorded, and transcribed verbatim.

Data analysis With the aid of a research management tool, Atlas-Ti, the data were coded and organized into themes that could then be compared and contrasted. The data analysis process involved three steps including: (i) a descriptive step that identified categories to help the authors understand the experiences and perspectives of the key informants; (ii) a conceptual step that used principles of grounded theory to link the identified categories and themes to ethical principles and regulations of clinical research; and (iii) a comparative step that compared experiences and perspectives within and across the two stakeholder groups. After conducting 80 interviews no new information was emerging from either clinicians or coordinators; it was determined that saturation had been achieved and so the interview process was suspended.

Results

Throughout the article, we use verbatim quotations from clinicians and research coordinators to illustrate key findings. The comments offered by clinicians are identified by the letter P and a number. The comments by coordinators are identified by the letter C and a number.

Most respondents, 72 of 80 (90%), worked in blended hospital-center or hospital-clinic settings where the center or clinic physicians had defined relationships including admitting privileges with the local hospital. Areas of specialty included allergy, cardiology, endocrinology, family practice, gynecology, neurology,

oncology, orthopedics, and urology. Nearly all of the respondents 76 of 80 (95%) reported that their patient base included a sizeable rural population, ranging from 50 per cent to 100 per cent. Bringing clinical trials into community settings was seen as offering important benefits to people who live in non-metropolitan areas. Representative of this perspective one research coordinator explained:

> So, we continue to do it because it's the right thing for our patients. And now we've become known for our patients not having to travel and they get that cutting edge care here in a rural setting where before they thought they'd have to drive hours to get it. So, I think that's part of the reason that we really have maintained what we've done and continue to push; our patients are our biggest advocate and they feel very thankful that we can offer this to them so close to home and offer them chances that they otherwise wouldn't have. (C14)

Building on the trust that develops between clinicians and patients in community settings, another coordinator noted, "I'm really not sure how to explain it. But we've become a familiar face to them and they like having that familiarity to help walk them through treatment." (C8). This perspective was reinforced by a doctor who responded, "We take interest in them and they take interest in us. And so our relationships are stronger. So when we do ask them, you know, they trust us already." (D31).

All of the clinician/investigators had received training in a health-related field such as medicine, nursing, or pharmacy. While most of the coordinators also reported background training in a health-related field, 12 respondents had received training in a non-health field. Most of the coordinators (28 of 42 or 66%), and a majority of the clinicians (23 of 38 or 53%), reported that they had never received any formal training in research methods. When asked to describe their training in research ethics, a majority of the coordinators (25 of 42 or 59%) reported some ethics training, primarily through an on-line course such as the Collaborative Institutional Training Initiative (CITI). Among the clinicians, fewer than half (17 of 38, or 47%) reported any training in research ethics.

Nearly all of the respondents conducted industry sponsored trials. The study budget was an important consideration when agreeing to accept a study. Indeed most acknowledged that clinical trials provided an important source of revenue for clinicians and institutions. Some conducted both federally funded and industry funded trials, but reported that the federally funded studies were often so poorly funded that the researchers found they could ill afford to take those trials and had to balance research interests with economic realities. A majority of the respondents (65%) had affirmed that the practice of requesting a donation of specimens from trial participants for genomics or biobanking was quite common. Representative comments include:

> [T]he first two studies we did, did not involve any genetic component, but since then nearly every one of them has. (C16)

> A lot of the studies have addendum consent that involves genetics. (C18b)
>
> Most of them actually do samplings for genetic testing … But they don't really know what to look for. (P2)
>
> The industry sponsored ones do. We always have – it seems like that's the new thing with all these studies is – you have your main study component and then there's a side component of that – whether the patients can – want to submit blood samples that will be used for genetic analysis and then future use samples for use down, you know, 20, 30 years down the road. (P13)
>
> But we are certainly seeing that more. I think the studies are far more complex. They're coming with kind of, you know, you have the main study and then they have all these, what do you want to call them, ancillary studies or whatnot, but other studies attached to them, like pharmacokinetics or – genetics. (C39)
>
> Almost 100 per cent of the time. (C34)

There was some hesitancy among those who said that their studies did not involve genetics. Within this group, most expressed uncertainty when trying to answer the question and expressed caveats such as "not yet," or "for now saying no." In some cases it was evident that the respondents said "no" because they did not consider the practice of asking for blood samples for biobanking as being part of a genetics association study. In other cases, respondents said "no" because the actual genetic research for which samples were gathered was not conducted in their facilities. The following representative comments showcase this uncertainty about the status of genetic research:

> No. Not at – well, we're just getting into the genetics. And then some of the industry trials, you know, they may involve some genetic portion, blood draws and things like that – through the industry trials. But we haven't done a whole lot. They're talking of starting some sort of biobank here. (C35)
>
> I'm not sure – I mean, I don't – I mean, there are some companion studies that, you know, involve tissue banking. Some of our cooperative group trials, you know, there probably are a few industry trials that we participate in that may collect things for pharmaco-genetics. I can't give you a number off the top of my head. I mean, I do know that there are compendium trials that, you know, patients can or cannot sign up for some tissue banking. (P25)
>
> I don't think so at this time. We do, I know, quite a bit of, you know, genetic counseling and referring, obviously, for genetic testing, but I don't see us participating specifically in any clinical trials. And I'm not aware of – the organization that we're gonna partner with, the [research network], you know, they have about 80 or so clinical trials. I'm not thinking they have any genetics, maybe some tissue banking and those types of things. But I don't see us participating necessarily in those types of trials. (P17)
>
> My own research, no, except we've done some multicenter trials. Sometimes there's a component when we collect specimens for future genetic research to be done by the study wide group. (P14)

Respondents were asked if separate consent forms were used when inviting participants to donate specimens for genetic studies. In a few cases a separate consent form was used, but this seemed the exception rather than the norm. Most reported that consent for such studies was woven into the main consent document. This approach was often described as a signature line or a box that could be checked in the general consent form. Explained one coordinator, "Some of them have a, you know, a separate section built into the main consent form to address that. So that, you know, where the patient wouldn't actually have to agree or not agree on the main consent form." (C23). When asked if genetic tests add value to a study, most respondents found it hard to articulate the value of the genetic components. There were notions that there would be benefits "down the road." But ideas, or understanding, of how the genetic data would be used seemed vague and distant. As one physician explained, "I think it is − I don't know." (P13).

Respondents were also asked if patients expressed concerns about privacy, confidentiality, or anonymity when enrolling in trials. Most (60%) said that participants, in general, seemed unconcerned about those issues. This was shown by the following comment: "I don't – my impression is that in our rural communities that hasn't been an issue." (C12). Those who acknowledged that trial participants sometimes appeared concerned (40%) described their efforts to assure patients that all necessary protections were firmly in place. This is shown by the following representative comment: "I tell them that we remove their names, phone numbers, addresses, socials, but we use their initials, their medical record number here, and their date of birth. I do tell them that because we do research trials, we have to have auditors come every couple years or whatever." (C19). When the researchers offer such reassurance, any concerns the trial participants may have had about biobanking appear to be allayed.

The general lack of understanding of the implications of genetics biobanking made it difficult for the respondents to even envision what kinds of resources or educational tools would help prospective participants make more informed decisions. Some believed that they did not need particular tools or resources to help explain genetic implications. As one physician explained, "No, because I don't really have to understand what I am doing when I am drawing. I send the samples to New York or wherever. I just have to be able to have it drawn on schedule and get it shipped out." (P26). Most participants, however, reported that they wanted resources, not just for patients, but for themselves as well. As one coordinator said, "Oh, yes. 'Cause I don't understand it very well either." (C20). At times the respondents seemed to be grasping in their efforts to find ways to make information about genetic testing more accessible. Explained one person,

> I can't tell them exactly how that information whether, you know, if it's genetic information or what have you, I can't tell them exactly how it's going to be used. And so, if I had, whether it was through perhaps, you know, a little flowchart or if it was something done in pictures to make it really simple or just some really down to earth examples of exactly how they're going to use this, including to some degree even the methods. (C16)

Discussion

This study sheds light on emerging issues that may not be well addressed by current regulatory approaches. When the Common Rule was first created, most clinical research was conducted in prestigious academic research environments by highly trained researchers. In today's research environment neither the clinician/researcher nor the coordinator may have a robust background in research methodology or research ethics. They are essentially gathering data for someone else's study and have limited knowledge about how, or if, the data will be used, analyzed, or stored. They are recruiting their own patients into the trials and believe that research participation provides important benefits to these patients. This backdrop seems to blur fundamental distinctions between research and clinical care.

The rapid advances in genetic technologies add a new layer of complexity, one that makes it hard for clinicians and coordinators to help patients make informed decisions about participating in clinical research. Most respondents did not seem to realize that genomic studies have changed the extent to which we are able to assure privacy, confidentiality, and anonymity. It is now possible, using various public data sets developed for both research and non-research purposes, to deduce the individual identity of some research participants. Further, electronic medical records, social media programs, and continual data sharing have blurred distinctions between public and private information. Although most respondents believed in the potential benefits of genetics research and biobanking and expressed hopes for individualized medicine at some point in the future, they seemed unprepared to deal with the ethical issues that can accompany studies with genetic and pharmaco-genetic components. They were generally "in the dark" with respect to how the blood or tissue samples they collected and sent away would be used. There were vague notions of future use. At times the inclusion of a genetic association study when part of a larger clinical trial went unnoticed. Consequently, most respondents were not worried about the implications of adding genetic components or where the samples go, how they are managed, or who might have access to them. Most also reported that trial participants expressed few concerns about participating in genetic studies. It seemed that the lack of concern expressed by patients was tacitly reinforced by clinicians and coordinators, who seemed to convey the message, "don't worry about it."

It is difficult to articulate with any specificity what researchers and participants should "worry" about when clinical trials include genetic association components. While the field of genetics is evolving, societal values about privacy, confidentiality, and anonymity are also evolving at a very rapid pace. Given the data sharing and data selling that permeate today's society, vast amounts of information about our habits, our behaviors, our preferences, and our locations are just keystrokes away. Most of this information gathering and exchange takes place without our consent; it is the price of living in today's society. We are no longer clear about what it means to protect privacy, confidentiality, and anonymity, or how important that might be. We do not know if frank discussions about the limits of assuring privacy, anonymity, and confidentiality would inhibit recruitment or willingness to enroll in clinical trial research. Nor do we know how participants might feel about the use of their personal genetic data for future commercial purposes. In short, we do not really know what matters at this time.

There are some limitations to this study as it was exploratory in nature. Although we sought to include a broad representation, we interviewed only those who were willing to engage in frank and detailed discussions about their involvement in the clinical research enterprise. Using the grounded theory methodology we reached a geographically diverse sample and thematic saturation, but may not have reached those who may have different experiences of clinical trial research. The published literature, however, lends support to the trends that emerged in this study, and so findings may be relevant to the growing number of sites that may choose to participate in clinical trials. The findings are also relevant to regulatory agencies and IRBs as they ponder the ethical challenges that can emerge when clinical research is conducted in non-academic settings. The findings certainly suggest the need for more research – and more discussion – before we can truly appreciate and then assess what it means to optimize the protection of human subjects and what, if any, special protections are needed when the clinical research conducted in community settings includes genetic components.

Our findings underscore the need to ensure that the regulations governing research on human subjects keep pace with the social and technological changes. It seems essential to discern legitimate concerns and find ways to convey to research subjects what is going on, what is possible, and what might not be possible in terms of protecting privacy, anonymity, and confidentiality. This endeavor requires the management of both conflicting and converging values − ones that support an open society and ones that ensure a closed one. If not very carefully managed, a great deal of tension and uncertainty could ensue. The stakes are high. It is critical to protect human subjects to sustain societal trust in the clinical research enterprise. If regulations do not keep pace with the technological and societal changes, they will become irrelevant and unenforceable.

Declaration of conflicting interests

The authors declare that there are no conflicts of interest.

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References

Appelbaum P (2010) Understanding "understanding": An important step toward improving informed consent to research. *AJOB Primary Research* 1(2): 1–3.

Appelbaum PS, Lidz CW and Grisso T (2004) Therapeutic misconception in clinical research: Frequency and risk factors. *IRB: Ethics & Human Research* 26(2): 1−8.

Bogdan RC and Biklen SK (2006) *Qualitative Research for Education. An Introduction to Theory and Methods*. Needham Heights, MA: Allyn & Bacon.

Bohannon J (2013) Genealogy databases enable naming of anonymous DNA donors. *Science* 339: 262.

Chen DT, Miller FG and Rosenstein DL (2003) Clinical research and the physician−patient relationship. *Annals of Internal Medicine* 138(8): 669−672.

Cook A and Hoas H (2011) Trading places: What the research participant can tell the investigator about informed consent. *Journal of Clinical Research & Bioethics* 2(8): 1–7.

Cook A and Hoas H (2013a) The protectors and the protected: What regulators and researchers can learn from IRB members and subject. *Narrative Inquiry in Bioethics* 3(1): 51–65.

Cook A and Hoas H (2013b) Clinicians or researchers, patients or participants: Exploring human subject protection when clinical research is conducted in non-academic settings. *AJOB Primary Research* (in press).

Creswell J (1998) *Qualitative Inquiry and Research Design: Choosing Among Five Traditions*. Thousand Oaks, CA: SAGE.

Fisher JA (2007a) Coordinating ethical clinical trials: The role of research coordinators in the contract research industry. *Sociology of Health & Illness* 28(6): 678–694.

Fisher JA (2007b) "Ready-to-recruit" or "ready-to-consent" populations? Informed consent and the limits of subject autonomy. *Qualitative Inquiry* 13(6): 875–894.

Fisher JA and Kalbaugh C A (2012) United States private sector physicians and pharmaceutical contract research: A qualitative study. *PLOS Medicine* 9(7).

Hayden E (2012) A broken contract: As researchers find more uses for data, informed consent has become a source of confusion. Something has to change. *Nature* 486: 312–314.

Iltis A (2006) Lay concepts in informed consent to biomedical research: The capacity to understand and appreciate risk. *Bioethics* 20(4): 180–190.

Johnson T (2005) *Snowball Sampling*. *Encyclopedia of Biostatistics*. New Jersey: John Wiley & Sons.

Karp D, Carlin S, Cook-Deegan R, et al. (2008) Ethical and practical issues associated with aggregating databases. *PLOS Medicine* 5(9): 1333–1337.

Klein JE and Fleischman AR (2002) The private practicing physician investigator: Ethical implications of clinical research in the office setting. *Hastings Center Report* (July−August): 22–26.

Lin Z, Owen A and Altman R (2004) GENETICS: Genomic research and human subject privacy. *Science* 305(5681): 183.

Lunshof J, Chadwick R, Vorhaus D and Church G (2008) From genetic privacy to open consent. *Nature Reviews Genetics* 9(5): 406–411.

Malin B, Loukides G, Benitez K and Clayton E (2011) Identifiability in biobanks: Models, measures, and mitigation strategies. *Human Genetics* 130(3): 383–392.

Morgan D and Krueger R (1997) *Qualitative Data Analysis: An Expanded Sourcebook*. Thousand Oaks, CA: SAGE.

Morreim H (2009) The dirty little truth: We want them to understand, but not really. *The American Journal of Bioethics* 9(2): 9–22.

Murphy J, Scott J, Kaufman D, et al. (2009) Public perspectives on informed consent for biobanking. *American Journal of Public Health* 99(12): 2128–2134.

National Human Genome Research Institute. Genome-Wide Association Studies. Available at: http://www.genome.gov/20019523 (accessed: 8 April 2013).

Resnik DB (2009) Do informed consent documents matter? *Contemporary Clinical Trials* 30(2): 114–115.

Rodriguez L, Brooks L, Greenberg J and Green E (2013) The complexities of genomic identifiability. *Science* 339: 275–276.

Sand S, Kaasa S and Loge JH (2010) The understanding of informed consent information – Definitions and measurements in empirical studies. *AJOB Primary Research* 1(2): 4–24.

Schwartz V and Appelbaum P (2008) Improving the quality of informed consent to research. *IRB: Ethics & Human Research* 30(5): 19–20.

Shuchman M (2007) Commercializing clinical trials – Risks and benefits of the CRO boom. *New England Journal of Medicine* 357(14): 1365–1368.

Snyder L and Mueller P (2008) Research in the physician's office: Navigating the ethical mine field. *Hastings Center Report* 38(2): 23–25.

Strauss A and Corbin J (1998) *Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory*. Thousand Oaks, CA: SAGE.

US Department of Health and Human Services (1991) *Federal Policy for the Protection of Human Subjects ("Common Rule")*. Available at: http://www.hhs.gov/ohrp/humansubjects/commonrule/ (accessed 4 April 2013).

Wechsler J (2007) Central vs. Local: Rethinking IRBs: Regulators and sponsors encourage alternative review models to fit a growing research enterprise. *Applied Clinical Trials*. Available at: http://www.appliedclinicaltrialsonline.com/appliedclinicaltrials/article/articleDetail.jsp?id=401619 (accessed 6 April 2013).