

APPLIED  
CLINICAL TRIALS

# Protecting Subjects: The IRBs Next Steps



## OHRP's Response that it Agrees with FDA on the Benefits of a Single, Central IRB may Indicate Well-Needed Change

# Confidence in the Central IRB

### *Applied Clinical Trials'* Editors

**A**t the end of April, the Office of Human Research Protection (OHRP) at the Department of Health and Human Services (HHS), posted on its Web site a response to a medical center regarding the use of a centralized Institutional Review Board. The center was inquiring into OHRP's parity with the FDA in regard to the use of the external or central IRB.

In its post, the OHRP says in response that it "fully agrees with the FDA's position on the benefits of relying on a single central IRB for multicenter research."

The letter that was sent in for OHRP clarification on the use of central IRBs can be read here: <http://www.hhs.gov/ohrp/policy/correspond/Menikoff20100413letter.html>.

The OHRP response was swift, and located here: <http://www.hhs.gov/ohrp/policy/correspond/Menikoff20100413letter.html>, and does make reference to the FDA's March 2006 guidance document "Using a Centralized IRB Review Process in Multicenter Clinical Trials" found here: <http://www.fda.gov/RegulatoryInformation/Guidances/ucm127004.htm>.

The OHRP basically says in its response that it is "taking steps to address institutions' concerns about relying on an IRB external to the institution."

What can be inferred from these exchanges between a large health system looking to streamline its IRB oversight and the department that oversees research that is supported by the HHS?

First is the fact that outsourcing has become a way for many different types of

organizations to streamline costs and gain efficiencies. Which apparently is true for even a health care delivery system located in the Southern United States.

What can also be true, as has been suggested, is that the OHRP response would actually help institutions feel comfortable and thus more likely to use a central or external IRB.

### **Next Steps**

Last year, independent IRBs took a hit when one of these organizations was caught in an undercover sting operation that led to a Congressional hearing and the company's subsequent decision to close its business. These independent IRBs, for-profit entities, all felt the negative perceptions that came out of public government hearings.

However, rather than dwell on a less than stellar situation, many IRBs took this event, examined their own policies and processes, changed them if needed, and moved ahead with a stronger resolve in their role of protecting subjects. We learned this from the contributors to last year's special insert titled *Protecting Subjects: The IRBs Role Today*.

One year later, IRBs obviously still take seriously their part in the vital chain that protects subjects in clinical research. And they have grown based on new approaches and strategies they have adopted in the past year.

The IRBs participating in this month's special insert, *Protecting Subjects: The IRBs Next Steps*, offer their opinion on how the central or external IRB can best

help sponsors. In the insert, they also shed light on a variety of topics, including the importance of communication and language in the IRB process; compliance and what that means as subject protection progresses; education and certification to achieve a level of confidence in research protection; a review of all the parties involved in drug development and how their roles help achieve subject protection; and more.

Like most in the drug development industry, IRBs need to grow quickly in the face of change. From this insert, we can see they are doing this successfully.

## Internet References

**Self-Evaluation Checklist for IRBs**  
[http://appliedclinicaltrialsonline.findpharma.com/IRB/FDA\\_Checklist](http://appliedclinicaltrialsonline.findpharma.com/IRB/FDA_Checklist)

**Association for the Accreditation of Human Research Protection Programs** <http://www.aahrpp.org>

**Office of Human Research Protection** <http://www.hhs.gov/ohrp/>

**FDA, Frequently Asked Questions, Statement of Investigator (Form FDA 1572)** <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM214282.pdf>

### **APPLIED CLINICAL TRIALS ARTICLES RELATED TO IRBS, ETHICS COMMITTEES, AND THEIR FUNCTION:**

**Protecting Subjects: The IRBs Role Today** <http://appliedclinicaltrialsonline.findpharma.com/irbrole>

**Differences in Standards for IECs**  
<http://appliedclinicaltrialsonline.findpharma.com/iec>

## CONTENTS

### **2 Confidence in the Central IRB**

*Applied Clinical Trials'* Editors

### **4 The Role of IRBs in Research**

Cami Gearhart

### **6 IRB Inconsistency?**

Erica Heath and Terri Majors

### **8 Principles of Ethical Review**

Jack Corman

### **10 Partnering to Ensure Compliance**

Lynn A. Meyer

### **12 Investigator Awareness**

Alycia Huston and Charlotte Stewart

### **14 Contributor Index**

COVER PHOTO: JON FEINGERSH PHOTOGRAPHY INC/  
BLEND IMAGES/GETTY IMAGES

## IRBs are Essential to Ethics Review, but Other Parties Have a Role to Play in Subject Protection

# The Role of IRBs in Research

Cami Gearhart

**W**hat is the role of the institutional review board (IRB) in research today? The IRB's role is probably both more important and more narrow than many realize. The IRB's role is important, as the oversight provided by the IRB continues to prompt important modifications to proposed research. But the IRB is only one of many components in the framework of human subject protection. Other entities—such as data monitoring committees, site monitors, and research institutions—also help ensure human subject protection with powers complimentary to the IRB's.

The role of the IRB is dictated by federal regulations that were finalized in 1981.<sup>1</sup> The tragedies of research trials of prior years, especially the Tuskegee syphilis trial, motivated the regulatory requirements for ethics review.<sup>2</sup> The ethics review provided by IRBs continues to be important and IRBs often insist on modifications to proposed research, including changes to the protocol, consent form, and recruitment materials. Some examples include:

- A multisite protocol proposed that a study be pursued in an African-American pediatric population. When the ethics review board asked for justification of the racial requirements, the study was modified to remove racial parameters.
- A protocol involving individuals with multiple life-threatening diagnoses proposed that participants be allowed to reach risky levels of clinical lab values before rescue medication would be utilized. The ethics review board insisted

that rescue medication be available at less aggressive lab values in closer accordance with standard treatment levels.

- A proposed consent form submitted with a protocol failed to include a reference to an irreversible side effect known to occur in a small percentage of individuals using the study drug. The ethics review board modified the consent form to describe that risk.

A recent study suggests that IRB review also is important in improving the accuracy of consent forms.<sup>3</sup> The researchers reviewed consent forms used in 215 studies in one department of a major academic center from 1978 through 2002. In the early consent forms evaluated in the study, which dated back to 1978, more than 54% had discrepancies with the protocol. Most of the discrepancies understated the risks of the study or study drug. By the time the researchers reached consent forms dated 2002, they found no discrepancies.

Nevertheless, the IRB is not solely responsible for protecting research participants. One important mechanism under FDA regulations is the monitoring of safety data. This monitoring can take many forms: a committee within a sponsor, a division within a contract research organization (CRO), or an independent committee complete with bylaws and SOPs.<sup>4</sup> The IRB does have a role under federal regulations to ensure that an appropriate data monitoring plan is in place for each research study,<sup>5</sup> but the data monitoring committee (DMC) itself has powers beyond the powers of an IRB in assessing safety data. As stated by the FDA, “[a] DMC...generally

has access to much more data than the IRB during the trial, including interim efficacy and safety outcomes by treatment arm, and makes recommendations with regard to the entire trial. A trial may have multiple IRBs, each responsible for the patients at a single site, but only one DMC.<sup>4</sup>

Another set of important players in FDA-regulated research are site monitors. Site monitors, or clinical research associates, are individuals trained and often certified<sup>5</sup> to monitor compliance by investigators. FDA regulations specify that sponsors are required to select qualified monitors to monitor the progress of an investigation as well as compliance with the protocol and regulatory requirements.<sup>7</sup> In today's era of budget cutting, IRBs rightfully might question whether monitors are visiting sites as frequently as they should. Again, however, monitors have a role beyond that of the IRB to enter a site and oversee site activities. As such, monitors are able to provide a level of oversight above and beyond an IRB's regulatory or logistical capabilities.

Finally, we should not ignore the oversight role of the business structure of the research site or local institution itself. Respondeat superior (or, "let the master answer") is a legal doctrine that an employer is generally responsible for the actions of employees when those actions are performed within the course of employment. Under this doctrine, academic centers have a role in training and supervising faculty and students, and clinics and other research organizations have a role in training and supervising their staff. Related legal doctrines make hospitals responsible in some circumstances for physicians with admitting privileges. At times, institutions have shifted training and compliance responsibilities to their IRBs. More recently, however, some institutions have distinguished their training and compliance obligations as employers from the ethics review obligations of their IRBs.

This is not to say that the network of human subject protection cannot be improved. All of the entities described herein are vulnerable to conflicts of interest, budget cuts, and other pressures. It is critical that each of these oversight entities is in turn overseen by adequately funded government agencies and third-party certification agencies, such as the Association for the Accreditation of Human Subject Pro-

## **FDA regulations specify that sponsors are required to select qualified monitors.**

tection Programs. Nevertheless, the overlapping obligations of the IRB, the DMC, site monitors, and employers provide an impressive set of protections. In our imperfect world, the safety net of human subject protection provides multiple layers of protection for participants in clinical trials.

## **References**

1. See 21 CFR Part 56 and 45 CFR Part 46.
2. S. Chodosh, "A Unified Human-Research Protection Program," from E. Bankert and R. Andur, *Institutional Review Board: Management and Function* (2nd edition, 2006) p. 13.
3. I. Albala, M. Doyle, P.S. Appelbaum, "The Evolution of Consent Forms for Research: A Quarter Century of Changes," *IRB: Ethics & Human Research*, 32 (3) 7-11 (May-June 2010).
4. Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committee, OMB Control No. 0910-0581, p. 2 (March 2006).
5. 21 CFR 56.111(a).
6. The Association for Clinical Research Professionals offers a CRA certification exam ([www.acrpn.org](http://www.acrpn.org)) and the Society of Clinical Research Associates offers a Certified Clinical Research Professional exam ([www.socra.org](http://www.socra.org)).
7. 21 CFR 312.50; 21 CFR 312.53(d).

**Cami Gearhart, JD**, is Chief Executive Officer of *Quorum Review IRB*, Seattle, WA, [www.quorumreview.com](http://www.quorumreview.com).

## Adding Clarity, Education, and a Clearly Defined Language to the Research Community is the Best Solution

# IRB Inconsistency?

Erica Heath and Terri Majors

**A**n often asked question within the research community is, “Why are IRBs inconsistent?” As with most IRB decisions, the answer has several dimensions:

- IRB regulations are a framework
- IRBs are composed of individuals
- IRBs exist within a larger culture
- IRBs exist in a changing world.

In April 2010, the Ethical Review Committee (ERC) and Independent Review Consulting (IRC) began functioning as a combined entity, Ethical & Independent Review Services (E&I). This merger created a unique opportunity/challenge to closely examine each aspect of the IRB operations and processes to identify possible inconsistencies.

With many years of review experience, each IRB had developed within their own culture. Despite following the same regulations and being grounded in a common core value of the protection of subjects, we found disparities in semantics and at times a variance in philosophy. Usually the difference was identified through its reflection in operational details. Of course, the frustrations and complexities we faced are not an exclusive outcome of the blending of two IRBs. We know it reflects the same frustrations felt by many people interacting with multiple IRBs. We are hoping that some of the issues we identify will be helpful.

### Human Subject Regulations are a Subjective Framework

The subjective nature of human subject regulations requires IRBs to develop their

own set of experiences and precedent. Regulations give us very subjective definitions such as “minimal risk,” and subjective review criteria such as “informed consent will be appropriately documented.” Objective, specific rules could not be written for each situation. Instead, the regulators asked committees to consider these difficult questions for each study and come to a decision.

For example, what is a minimal risk of harm?<sup>1</sup> Is what is encountered in daily life different in Missouri than in California? Is the risk relative to the everyday experience of the subject, such as a child with cancer as compared to a healthy child? We find that perception of risk is constantly challenged. There is no table of “standardized” risks, and it likely cannot be developed given that much of the consideration is contextual.

### Each IRB is a Group of Individuals

Each decision is an amalgamation of the opinions, experiences, and culture of individuals. Decisions are filtered through this unique composition. Typically, there is a range of beliefs. As membership changes over time, the perceived “face” of the board alters.

Each individual contributes to the protection of the human subject within the framework of his or her background. Perhaps what seems like inconsistency in their directives is actually an expression of individual thought applied to specific situations including the opportunity for a change in interpretation through additional experience.

## **IRBs Exist within a Larger Culture**

Each IRB serves within the cultural framework of its parent institution. Each institution has its own personality and differentiates itself from like institutions. These personality differences result in IRB differences, which are reflected in the language, processes, and even the forms. Interacting with each of these IRBs may reveal that the inconsistencies can be traced to the culture in which the IRB exists.

For example, some institutions are more risk accepting than others. Some are rigid, while others are more flexible. The federal regulations that provide the minimum standard are the foundation. From there, each institution is expected to build a program of protection—including their IRB—in ways that meet their unique personality.

## **IRBs Exist in a Changing Environment**

Of course, IRBs must be responsive to the research culture that is not a stagnant environment. New and revised FDA and OHRP guidance, FDA warning letters and OHRP determination letters, AAHRPP accreditation standards, changes in state laws, and even congressional hearings contribute to the changes in the IRB domain.

An element of the IRB's changing environment is brought by the different requirements made by sponsors. For example, the length of consent forms has expanded over the years, often as a direct result of the sponsor's required language inclusions.

In other arenas, FDA has added REMS (Risk Evaluation and Mitigation Strategies) requirements and expanded access for investigational drugs. The economy has affected the numbers of studies funded both federally and privately. For many IRBs, the kind of research that represented the norm two years ago has changed. Does this affect the IRBs? Most definitely. IRBs must be open to new understanding and interpretations, not limited by "the way

they have always done it," while keeping in sight the purpose for their very existence.

## **How Do IRBs Help You Balance these Perceived (or Real) "Inconsistencies"?**

The solution begins with clearly defined language. Many IRBs, including E&I, include a glossary on their Web site. We must make consistent effort to communicate clearly and be prepared to offer clarity about why a decision was made; what appears to be inconsistency may then be more easily understood. If a decision is in-

## **For many IRBs, the kind of clinical research that represented the norm two years ago has changed.**

consistent with a prior decision, there may be a reason or a mistake. The IRB should hear from you and should listen.

In striving for better communication and a common language between the parties involved in conducting research, each interaction with a sponsor, investigator, or site coordinator is an opportunity to provide added clarity and education. In community, we can be more effective in developing a better understood language that has a greater likelihood of strengthening the protection afforded each subject.

Out of E&I's merger, we have learned there isn't always just one "right" way and by honoring and understanding our differences, we become a more effective IRB.

## **Reference**

1. Minimal risk means that the probability and magnitude of harm or discomfort anticipated are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations/tests [21 CFR 50.3(k)].

*Erica Heath, CIP, and Terri Majors, CIP, are Directors of Ethical and Independent Review Services, San Anselmo, CA, and Independence, MO, [www.eandireview.com](http://www.eandireview.com).*

## Addressing the Need for all Key Stakeholders to Move Beyond the Dysregulation of Research to More Ethical Research

# Principles of Ethical Review

Jack Corman

“**T**o preserve public trust in research, the scientific community must go beyond a culture of compliance—it must strive for a culture of conscience—one in which we do the right thing not because we are required to, but because it is the right thing to do, a refrain now echoed frequently throughout the research community.”—Greg Koski, *Outgoing Director, Office of Human Research Protection (OHRP), 2002.*

### Where Have We Been?

The fundamental reasons for the establishment of ethical review of research by a group external to the research are of course well known. The Nuremberg Code established the basis for modern human research protections, which were extended by the Declaration of Helsinki in 1964 to specify independent review was required, that is: “The design and performance of each experimental procedure...should be clearly formulated in an experimental protocol...submitted...to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence.”

Following the devastating revelations of the federally funded Tuskegee airmen’s syphilis study, the National Research Act established a National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, resulting in the landmark Belmont Report. The Belmont Report in turn serves as the foundation of U.S. federal legislation

governing FDA regulated (21CFR312, 50, 56, 812, etc.), and U.S. federally funded research (45CFR46, the “Common Rule”). So, for more than 30 years, a regulatory requirement for IRB review of research with humans has existed, compliance with which “is intended to protect the rights and welfare of human subjects...”<sup>1</sup>

### Where Are We Now?

We stand at a crossroads in research with humans, as a maelstrom of public attention has been focused on the practices of pharmaceutical companies and the clinical research they sponsor and resulted in an evermore onerous and costly research oversight system. This attention, welcome or not, balanced or not, includes sharp criticism of regulatory agency oversight mechanisms and their apparent failure to protect research integrity and subject well-being. This criticism in turn has led to such an intense focus on compliance with regulations rather than principles of ethical review and conduct of research, that many thought leaders have concluded the system, rather than increasing research protections, has passed the point of diminishing returns. In 2007, Norman Fost & Robert Levine, for example, wrote:

“The regulatory system for protecting human subjects in research in the United States is increasingly dysfunctional...Over the past decade, the oversight of IRBs has been characterized by increasing requirements for meticulous documentation of compliance with narrow interpretations of regulations and policies, often with punitive sanctions, accompanied and perhaps

exacerbated by a drumbeat of assertions that the regulatory system is broken... Many requirements imposed by federal agencies, and now by the accreditation process, have little relationship to the protection of human research participants... Inflexible requirements for adherence to narrow interpretations of every word in regulations and other policies have led to a system that is more concerned with protection of the institution than protection of human research participants. The cost of the system is increasing without evidence of a return on investment with regard to protection of patients and other research participants...”<sup>2</sup>

Has the situation improved since then? Hardly. The recent GAO sting operation involving Coast IRB and Congressional accusations of inadequate FDA and OHRP oversight of research have led to a government crackdown that, judging by recent warning letters, focuses virtually exclusively on narrowly restrictive regulatory compliance. AAHRPP accreditation requirements have become ever more arbitrary, severe, and restrictive; rather than contributing to the creation and maintenance of a “culture of conscience,” it seems the current accreditation process is contributing to the “culture of compliance” and fear. How this will materially contribute to improved protection of human research subjects and more ethical research is difficult to see.

### Next Steps

IRBs today are faced with many challenges not foreseen when they were first created, and which threaten their ability to effectively do their duty in a regulatory construct that is over 30 years old—social media, novel recruitment and retention strategies, adaptive and other new clinical research designs, nanotechnology, stem cell and reproductive re-

search, and legalistic consent forms and processes are just a few.

Regulatory mechanisms are, by their nature, reactionary and seldom able to change quickly to meet challenges presented by the rapid evolution of society, science, and technology. IRBs must be far more proactive to identify emerging trends in human research that pose new ethical challenges and to create flexible mechanisms that improve the ethical quality of the review and conduct of human research to adapt quickly to changing needs.

At present, our oversight system is governed by a paradigm that measures regulatory compliance but not ethical quality of review. It does not readily permit IRBs sufficient flexibility to adapt quickly to new challenges. Such an ethical quality measure, intelligently developed and implemented, is sorely needed.

IRBs and their organizations, for example, PRIM&R and the Consortium of Independent Review Boards (CIRB), together with sponsors, researchers, regulators, and especially accreditation bodies like

**At present, our oversight system is governed by a paradigm that measures regulatory compliance but not ethical quality of review.**

AAHRPP, must work to do everything possible to move past obsession with regulatory compliance and build an effective and accountable system of oversight that measures ethical outcomes. The time is now.

### References

1. 21 CFR 56.101(a).
2. N. Fost and R.J. Levine, “The Dysregulation of Human Subjects Research,” *Journal of the American Medical Association*, 298 (18) 2196-2198 (2007).

**Jack Corman** is President of IRB Services, Ontario, Canada, [www.irbervices.com](http://www.irbervices.com).

## Some Next Steps Would Require the Support of Sponsors and Institutions in Order to Become Accepted Practice

# Partnering to Ensure Compliance

Lynn A. Meyer

**C**ompliance is a common goal among all involved in clinical research. Standard Operating Procedures (SOPs) are designed to describe the methods and processes utilized by an organization to ensure compliance with federal regulations. Federal agencies, sponsors, and contract research organizations routinely inspect IRBs and perform site evaluation visits to determine whether it has adequate policies and processes in place to comply with federal regulations. In addition, most organizations involved in clinical research have numerous SOPs of their own to ensure compliance with the many regulations they must adhere to.

But what steps are currently being taken by federal agencies to ensure adequate training of those conducting and assisting in research projects? When it comes to demonstrating education regarding federal regulations related to the protection of human subjects, what is required? Currently, there is no federal regulatory body that requires a principal investigator and/or staff to document that they have this type of training.

Existing opportunities available to demonstrate knowledge and experience include certification programs and online modules for researchers, research staff, and IRB members and staff, as well as accreditation of human research protection programs. It is my understanding that some sponsors require evidence of clinical research training, if not, certification of principal investigators. Why is this not a regulatory requirement, one might ask?

One of the next steps to be taken by IRBs might include requiring documentation of current clinical research training. For this to become an acceptable practice would require the support of sponsors and institutions, making it a partnering effort. I believe there is a need for strengthening the relationship among investigators, sponsors, institutions, and IRBs, which would result in improved efficiencies.

### What is Partnering?

Webster's Collegiate Dictionary defines partner as "one that shares" and "a member of a partnership." Establishing ongoing relationships can only be achieved when all partners have a clear understanding of expectations, accept responsibility, provide quality service, are responsive, and maintain constant communication.

In an effort to enhance and ensure the protection of the rights and welfare of study participants it is the responsibility of many partners: the sponsor, principal investigator, study staff, and, of course, the IRB. Therefore, it would seem to make sense that as partners, all responsible parties would form a strategic relationship to ensure compliance of all entities.

### Relationships

For many years, and perhaps still today, IRBs have been viewed as an obstacle to be overcome by investigators as well as sponsors. IRBs often have no face and are an unseen entity that projects authority and dictates changes to research.

IRBs can create and develop relationships with site investigators by employ-

ing knowledgeable and friendly staff that is readily available to provide regulatory guidance and answer questions quickly without being judgmental.

Independent IRBs continue to establish effective relationships with institutions to alleviate the increased burden being experienced by the IRB staff. These relationships are developed through respect and understanding of a common goal shared by these organizations.

Sponsors can nurture a partnership with an IRB by communicating with the IRB as early as possible, discussing expectations, and involving the IRB in investigator meetings. An IRB presence at an investigator meeting could serve several purposes. The mystery of the invisible IRB would be eliminated; regulatory training could be incorporated; investigators and/or study coordinators could receive instruction regarding the specific processes and procedures utilized by the IRB, which would ultimately enhance efficiencies. All of this interaction serves to build confidence and trust among the entities.

### **Ensuring Compliance**

**Training**—Suggested methods for ensuring compliance include engaging knowledgeable IRB staff and committee members and utilizing experts when needed as well as providing ongoing training. Many online courses provide a certificate of completion. IRB committee members and staff might be required to complete specific topics each calendar quarter. This might be required in order to maintain active committee status or be a performance standard for IRB staff. It is critical that all persons involved with research studies regularly review new and revised SOPs in order to remain current.

**CAPA**—A corrective and preventative action program (CAPA) can be an effective method of identifying internal and external noncompliance issues that can result in

process improvements. It also assists in identifying the root cause that can result in process improvements and learning opportunities as well as helping to prevent similar problems in the future.

**Quality Assurance and Quality Control**—Developing and implementing exceptional quality assurance and control processes is essential to ensuring compliance. Thoroughly examining information provided in clinical study submissions along with confirming critical information, such as medical licenses and debarment lists is essential for ensuring compliance. Detailed checklists have proven invaluable when performing quality assurance. Equally as important is quality control, which should be performed on all documents. Once again, the use of a detailed checklist ensures consistency while maintaining focus and further ensuring compliance.

**Sample Informed Consent Documents**—It is a common practice for IRBs to provide a template for informed consent that contains all of the basic elements as well as the additional elements of consent. Furthermore, these templates often include specific language required by the IRB for particular situations. Use of these templates typically results in only minor revisions required by the IRB and are reviewed more efficiently.

### **Sponsors can nurture a partnership with an IRB by communicating with the IRB as early as possible.**

Human research is a field that relies on accuracy, honesty, individualized attention to details, and the ability to respond quickly and effectively in a rapidly changing professional landscape.

**Lynn A. Meyer, CCRP**, is Managing Partner of *IntegReview Ethical Review Board*, Austin, TX, [www.integreview.com](http://www.integreview.com).

## An Educated Investigator Sets the Stage for High-Quality Clinical Research that Places the Subject First

# Investigator Awareness

Alycia Huston and Charlotte Stewart

In the research arena, the Principal Investigator is ultimately responsible for all aspects of a research project. Principal Investigators are charged with conducting objective research that generates independent, premium, and reproducible results. The Principal Investigator is responsible for the management and integrity of the conduct, and reporting of the research project and for managing, monitoring, and ensuring the integrity of any collaborative relationships.

Additionally, the Principal Investigator is responsible for the direction and oversight of compliance of his or her research personnel, and other related aspects of the clinical research project. Most importantly, they must ensure that the research is conducted in a manner that protects the rights and welfare of human research participants in accordance with Federal regulations and sponsoring agency policies and procedures.

Ongoing training and education for the Principal Investigator and key research staff is vital to ensure that research studies are conducted in accordance with applicable federal regulations such as GCP, and that the Principal Investigator and the research staff have a solid understanding of their respective responsibilities. The regulations that govern research may not be “changed” but are certainly clarified and guidance is provided.

As Principal Investigators are fully responsible for the conduct of the research and the protection of human subjects, it is necessary that they fully understand the laws and regulations that govern re-

search. The purpose of these regulations is to protect those that choose to place themselves at risk for the advancement of new and better drugs, devices, and procedures. It is only fitting then that the Principal Investigator is well versed in these laws and regulations to be able to provide these protections.

### Building Blocks of Success

Many Investigators believe that their main role in clinical research is to carry out the protocol, verbatim, rather than the protection of the human subjects. Education of Principal Investigators reminds them of their charge that their subjects come first and foremost.

As an example, the purpose of Informed Consent is to provide a written description of the risks and benefits of study participation. This also gives the Investigator an opportunity to communicate with the study subject and explain any procedures that may not be immediately understood. This gives the subject and the researcher the opportunity to converse and build a rapport, opening the door for more valuable conversations in regard to effectiveness and/or possible side-effects of study products.

The written Informed Consent has regulatory requirements. An investigator is required to know what these requirements are. Even though an Independent Review Board (IRB) has been engaged to assist in the oversight of the study, the Investigator, as the individual chosen to conduct the study, must also be educated in what these requirements entail.

It is the responsibility of the IRB to provide an Informed Consent Form that is clear and understandable to the person to whom it will be presented. The ultimate responsibility of whether or not the document contains all the required elements lies with the Investigator. The IRB approved document is to be reviewed by the Investigator upon finalization from the IRB to ensure that all required elements are present.

### **Potential Pitfalls**

As an IRB, it has been found that non-compliance of Investigators is due more to a lack of understanding on their part of the current regulations rather than an intention to break the rules with no regard for consequences. In most instances, the Investigator has either forgotten what they have previously learned or their latest regulatory instruction is not current. This is why it is imperative that Investigators reacquaint themselves with the regulations that govern research at a minimum of every two years.

Conflict of interest is a very hot topic. Conflict has now been clarified to include Investigators, their families, and their staff. Conflict of interest includes much more than was initially published. Items published regarding the conflict of interest in clinical research includes much more than the regulations and is clarified in recent guidance:

- The opportunity for an Investigator to become an investor who would benefit financially from a positive outcome of an investigational product would also potentially add to their professional advancement and prestige.
- The opportunity to gain financially from speaking engagements, such as placing the investigational drug in a positive light.
- Acceptance of gifts provided from the sponsor or CRO to agree to take on a particular research project.

Continuing education has identified those items that were not readily brought to mind when IRBs and the duties of the Investigator were first established.

The use of investigational products, in conjunction with the use of human subjects in research, is much too valuable to the advancement of science not to provide all possible protections. The surest way to provide this protection is to keep those that are conducting the research well informed and properly educated. Noneducated researchers place persons unnecessarily at risk. If the rules of research are not followed, the collected

### **Noncompliance of investigators is due more to a lack of understanding of the regulations rather than an intention to break the rules.**

data could be disqualified and subjects would have been placed at risk with no positive result.

### **Mission Critical**

Education is not about completing modules and finishing programs, nor is it just about the education of the Principal Investigator. It is how we can all work together for the common goal of the protection of those subjects who have placed themselves in our care.

Research, in general, has been under additional scrutiny in recent months. It is imperative that we who are entrusted by the public with their welfare, treat that "gift" with the utmost respect. In the event of questions or problems, it is invaluable that education has been completed and maintained. This would further illustrate to study participants that their investigator is diligent in their practices.

*Alycia Huston is Chief Executive Officer and Charlotte Stewart is Chief Operating Officer at Aspire IRB, La Mesa, CA, [www.aspire-irb.com](http://www.aspire-irb.com).*

# Contributor Index

	NAME & CONTACT INFORMATION	AD PAGE*
	<p><b>Aspire IRB</b>            9320 Fuerte Drive            Suite 105            La Mesa, CA 91941  <b>Phone:</b> 619-469-0108  <b>Fax:</b> 619-469-4108  <b>Email:</b> email@aspire-irb.com  <b>Web site:</b> www.aspire-irb.com</p>	<p>43</p>
	<p><b>Ethical and Independent Review Services</b>            14400 E. 42nd Street            Suite 240            Independence, MO 64055  <b>Phone:</b> 816-421-0008                CA office: 415-485-0717  <b>Fax:</b> 816-356-2227                CA office: 415-485-0328  <b>Email:</b> lwilson@eandireview.com  <b>Web site:</b> www.eandireview.com</p>	<p>35</p>

 <p><b>INTEG</b> <i>i</i> <b>REVIEW</b> Committed to the Protection of Research Subjects</p>	<p><b>IntegReview Ethical Review Board</b> 3001 S. Lamar Boulevard Suite 210 Austin, TX 78704 <b>Phone:</b> 512-326-3001 <b>Fax:</b> 512-326-3446 <b>Email:</b> <a href="mailto:integreview@integreview.com">integreview@integreview.com</a> <b>Web site:</b> <a href="http://www.integreview.com">www.integreview.com</a></p>	41
 <p><b>IRB</b> INSTITUTIONAL REVIEW BOARD SERVICES</p>	<p><b>IRB Services</b> 372 Hollandview Trail Suite 300 Aurora, Ontario, Canada L4G 0A5 <b>Phone:</b> 905-727-7989 <b>Fax:</b> 905-727-7990 <b>Email:</b> <a href="mailto:info@irbservices.com">info@irbservices.com</a> <b>Web site:</b> <a href="http://www.irbservices.com">www.irbservices.com</a></p>	39
 <p><b>Quorum</b> REVIEW IRB</p>	<p><b>Quorum Review IRB</b> 1601 Fifth Avenue Suite 1000 Seattle, WA 98101 <b>Phone:</b> 206-448-4082 <b>Fax:</b> 206-448-4193 <b>Email:</b> <a href="mailto:CustomerRelations@quorumreview.com">CustomerRelations@quorumreview.com</a> <b>Web site:</b> <a href="http://www.quorumreview.com">www.quorumreview.com</a></p>	34

\*Ad page corresponds to the July 2010 *Applied Clinical Trials* issue.

**OFFICES**