

In the IRB World, An Application of Flexibility and Learning to Live with Shades of Grey is Helpful

Common Sense and the Rules

Erica Heath

IRC's tag line; dedicated to the protection of human subjects through application of laws, regulations, and common sense, can pose a challenge to live up to. After all, what to one person is a reasonable, common sense solution to a problem is, to another person, mission-creep, overkill, and indicative of a lack of understanding.

Why is common sense an issue? Rules are often considered to be either black or white, there can be little flexibility. IRBs, however, were created specifically to consider shades of grey. There are conflicts between science and rights and there are conflicts of mission. Without an underlying appreciation of resources, policies, and the uncommunicated choices and strategies of our partners, common sense can turn to Babel. Common sense helps reconcile multiple problems.

IRBs operate in a constrained regulatory world. There are the FDA's IRB and consent regulations and numerous ancillary regulations, the Common Rule, state rules, and of course HIPAA. Each institution and site has its own rules and culture.

A self-imposed constraint comes from accreditation. AAHRPP (Association for Accreditation of Human Research Protection Programs) requires an integrated Protection Program with the IRB integrated into an institutional protection network. Where there is a functional program, the IRB is able to pursue its original purpose: review of proposed or continuing studies. AAHRPP recognizes the individuality of each institution and simply asks for an integrated program. This means that each

IRB is unique, as is each sponsor and site. A central IRB such as IRC's cannot become fully integrated into the programs of multiple sponsors and sites but must know to whom to report issues.

Introducing common sense is like swimming upstream into a bureaucracy serenaded by "we have always done it this way." It is easy to go with the flow but, when we do, changes will never be made. At IRC we continuously seek to push the envelope on behalf of subjects to write sensible, readable, and understandable consent forms.

With rules seen as black or white, with each IRB, institution, sponsor, and site having different concepts, and all is chaos, how can common sense be introduced? If the following ideas are used in planning, presenting, and reviewing studies, perhaps some common sense will enter the process.

Live the Belmont Report. When the Belmont Report was written, doctors still sat on thrones and subjects rarely knew they were subjects. Belmont's authors tempered "Beneficence" with "Respect for Persons," thus requiring a balancing of science and subjects. Within IRBs and among sponsors and investigators, there are people who place a higher value on scientific inquiry and those who value the rights of subjects more highly. Frequently there is no right or wrong but simply a balancing of ethics and healthy inquiry.

Celebrate subjective rules. The regulations are very subjective: risks should be "reasonable" in relation to the "importance" of the knowledge that "may be expected"

to result, subject selection should be “equitable,” and informed consent should be “appropriately” documented. This gives remarkable interpretive leeway. The regulation writers in the 70s were well aware of this and it was intentional. They asked a diverse membership to use their judgment to work within this subjective framework in which absolute rules are inappropriate.

Use the rules flexibly. Is IRB approval required? Is the study FDA regulated? Are there human subjects? Can consent be waived? Assuming the answer and submitting an application to the IRB results in needing to comply with all aspects of the rules. Consider the need to obtain consent from anonymous donors. Consider the tone of recruitment materials used for a safety study of a marketed device. Knowing and using the rules correctly but flexibly can help avoid these conundrums.

Consider your mission and culture. Each party to research has a unique culture. A current example of conflict of mission is review of drug Safety Reports. IRBs have long considered these reviews to be onerous and without value. Industry has believed IRBs were required to review them for subject protection and rejection was seen as abdication of a duty. There are better alternatives being adopted that recognize both views. At IRC we seek to understand our clients’ mission and values.

Remember the subject. Subjects never read at a 5th or 8th grade level but at a range of levels. Some want to know every detail while others are satisfied with generalities. Within any given eligibility profile, some are more vulnerable than others. At IRC we seek a recruitment and consent process and form to match the circumstances. The more sensible the approach, the more subjects will benefit.

Share the rationale. When an IRB receives an investigators’ response to questions that says no alteration will be

considered, it is nice to know who made that decision and why. Is it because, “the FDA demanded it,” or because it has already been reviewed by 50 IRBs; was there a safety issue or design demand that wasn’t appreciated fully; or did some intermediary just want to avoid making waves with their client? Reviewing a request is much easier when the recipient knows the reason for the request. No IRB should be asked to assume facts.

Avoid over-reaction. With each warning letter posted on FDA’s Web site, each 483, each guidance, and following most conferences, there are reactions. Questions are added to submission forms and checklists. Another paragraph goes on the template consent form. These changes never go away! Finding ways to remain compliant while avoiding reactive maneuvers involves creative thinking.

Communicate. No protocol stands alone; it is the end result of many hours of strategy with many people. IRB members have only a slice of a larger picture. Failing to paint the larger picture may derail an otherwise easy approval.

IRC, as a remote, central IRB, cannot occupy the room down the hall as an academic IRB might. By using our common sense and by communicating and brainstorming solutions with our clients, we seek to create a partnership.

Living in a completely black and white world would be easier, but we live in a world painted in shades of grey. Taking advantage of the inherent flexibility built into many of the rules, clarifying motivations, and creating clear communication will help us maintain the range of color that makes research so interesting and exciting.

Erica Heath, CIP, is president of Independent Review Consulting, San Anselmo, CA, www.irb-irc.com.

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