Consistency in IRB Review
By David B. Resnik

Numerous studies have found that institutional review boards (IRBs) and research ethics committees (RECs) often treat similar studies differently with respect to how they evaluate risks, benefits, study design, the informed consent process, and other aspects of research (Silverman et al 2001, Hirshon et al 2001, McWilliams et al 2003, Angell et al 2006, Kimberly et al 2006, Mansbach et al 2007, Taljaard et al 2014, Higgerson et al 2014). For example, one study sent a survey to IRBs from 42 institutions participating in a multisite genetic epidemiology study. Thirty-one IRBs (74%) responded to the survey. Twenty-four responding IRBs (77%) categorized the study as more than minimal risk, therefore requiring full board review, while seven (23%) categorized it as minimal risk and allowed it to undergo expedited review. Three IRBs (10%) required four consent forms (adult, minor, parental and child assent), while 15 (48%) required two to three consent forms, and 10 (32%) did not require an assent form for children. There was also significant variation in the issues addressed by the different IRBs. Concerns expressed by the IRBs included genetic testing and biobanking (16, 52%), administrative issues (12, 39%), confidentiality (11, 35%), and reading level of the consent forms (7, 22%) (McWilliams et al 2003).

Concerns about inconsistency in IRB review are not new. Since the 1980s, various commentators, organizations and professional associations have urged government agencies and research institutions to promote greater consistency in IRB review (Goldman and Katz 1982, Rosnow et al 1993, Department of Health and Human Services 1998, Oakes 2002, Emanuel et al 2004, Hyman 2007, Menikoff 2010, Abbott and Grady 2011, Silberman and Kahn 2011). In this article, I explain why consistency in IRB review is important, discuss potential causes of inconsistency, and consider some strategies for promoting consistency.

Consistency in Ethics and Law

Consistency in ethics and law occurs when equivalent cases are treated in the same way. Cases are equivalent if their underlying relevant facts and circumstances are similar (Carr 1981, Dworkin 1986). Inconsistency occurs when cases with the same underlying relevant facts and circumstances are treated differently. For example, if John and Harold have both killed someone under similar circumstances, they should receive the same punishment. If they receive different punishments, this would be inconsistent. To treat similar cases differently without violating consistency, one would need to argue that the circumstances in the cases were different, e.g., John killed for revenge, whereas Harold killed as a result of reckless driving.

The obligation to maintain consistency in ethical and legal reasoning is often referred to as the “formal principle of justice” because it is a meta-principle for decision-making that has no material content (Aristotle 2003). While the principle says that similar cases should be treated the same, it does not state how they should be treated (Carr 1981). Material (as opposed to formal) principles are needed to provide normative content for ethical and legal decisions (Rawls 1971). For example, one might appeal to the material principle that the punishment should be proportional to the crime to justify sentencing John to life in prison for premeditated murder, while imposing a lighter punishment on Harold for killing as a result of reckless driving. Philosophers have defended a variety of material principles for
ethical and legal decision-making, which I will not discuss in detail here (see Pojman 2005, Dworkin 1986 for review).

There are at least three reasons why it is important to seek consistency in ethical and legal decisions. First, making decisions that are inconsistent could be viewed as irrational, since rationality demands that we abide by rules of logic, such as consistency. Many philosophers hold that practical decisions in ethics and law should be rational (Rawls 1971, Dworkin 1986, Pojman 2005).

Second, inconsistent decision-making may undermine material principles. For example, if one holds that punishments should be proportional to the crimes committed, and a person receives a punishment that is excessive, given his or her crime, then this inconsistency would undermine that principle. Likewise, inconsistent application of research rules and guidelines could undermine protection for human subjects. For example, if one IRB follows a guideline that requires a risky clinical trial to have a data and safety monitoring board (DSMB), but another does not, this inconsistency could undermine the principle that subjects in the study should not be exposed to excessive risks.

Third, inconsistent decision-making in an institutional (or organizational) setting can erode support for its rules, since people may decide to bend, break or manipulate rules if they believe they are being treated unfairly as result of arbitrary decision-making. Indeed, some studies indicate that employee perceptions of fairness in the workplace (organizational justice) are a key factor in promoting research integrity. Investigators who believed that their organization was treating them unfairly were more likely to report that they had engaged in unethical behaviors than those who believed they were being treated fairly (Martinson et al 2006, 2010).

**Inconsistency in IRB Review**

Consistency in IRB review involves treating equivalent research studies in the same way. Research studies are equivalent if they involve similar consent and recruitment procedures, aims and objectives, methods, designs, tests, target populations, and personnel. There are two types of consistency worth considering: intra-institutional (consistency within an institution) and inter-institutional (consistency between institutions). Both are important. Intra-institutional inconsistency occurs when an IRB treats equivalent studies at the same institution differently. For example, if an IRB classifies one study as minimal risk and another as more than minimal risk, when they both involve similar methods, procedures and tests, this would be inconsistent. If IRBs at different institutions classify the risk of equivalent studies differently, this would also be inconsistent (Hirshon et al 2002).

For the purposes of this discussion, it is useful to distinguish between real (or actual) inconsistency and perceived inconsistency. Real inconsistency occurs when the evidence indicates that an IRB has made inconsistent decisions. Perceived inconsistency occurs when it may appear to an outside observer that an IRB has made inconsistent decisions. Perceived inconsistency may or may not correspond to real inconsistency. Perceived inconsistency may occur even though the evidence does not indicate that the IRB has acted inconsistently. For example, if an investigator is not privy to a piece of information that formed the basis for an IRB’s decision to treat studies differently, then the investigator may view its decisions as inconsistent, although the full evidence indicates that they were not. Perceived inconsistency can be just a problematic for an institution as real inconsistency, since investigators who view IRB decisions as inconsistent may regard research oversight at an institution as unfair, which could erode support for the institution’s rules (Martinson et al 2006, 2010).
There are a number of potential causes of real or perceived inconsistencies in IRB decision-making (Edwards et al 2004). First, IRB members may interpret research regulations and guidelines differently as a result of differences in their backgrounds, e.g., their education, experience, race/ethnicity, gender, and cultural and moral values. Research regulations and guidelines include many words and phrases that are subject to interpretation, such as “risk,” “benefit,” “consent,” “vulnerable subject,” etc. Assessing research risks can be a thorny problem for IRB members. One study found that IRB chairs often disagree about the assessment of risks. Fifty-three percent of IRB chairs responding to a survey categorized an electromyogram as minimal risk or a minor increase over minimal risk, while 41% categorized it as more than a minor increase over minimal risk. Twenty-three percent of respondents considered allergy skin testing to be minimal risk, while 43% considered it to be a minor increase over minimal risk, and 27% viewed it as more than a minor increase over minimal risk (Shah et al 2004). Disagreements about whether to categorize a study as minimal risk, a minor increase over minimal risk, or more than a minor increase over minimal risk can lead to radically different IRB decisions concerning pediatric studies, since these categorizations determine the conditions under which it may be approved (Shah et al 2004).

Second, regulations and guidelines sometimes change. Although the Department of Health and Human Services (DHHS) human subject regulations (also known as the Common Rule) have not changed significantly in over 30 years, many guidelines and other regulations have (Department of Health and Human Services 2009). For example, the Food and Drug Administration (2014a) and the Environmental Protection Agency (2014) have significantly revised their human subjects regulations numerous times since the 1990s. The World Medical Association has revised its guidelines (“Declaration of Helsinki”) nine times since adopting them in 1964 (World Medical Association 2013). Additionally, many countries that previously did not have any human subject research regulations or guidelines have adopted some in the past two decades (Office of Human Research Protections 2014a). As a result, the oversight of research involving international collaborations continues to change.

Third, federal agencies frequently issue new guidance on how to interpret their regulations. For example, the Office of Human Research Protections (OHRP) and the Food and Drug Administration (FDA) have issued dozens of guidance documents in the last 20 years (Office of Human Research Protections 2014b, Food and Drug Administration 2014b). Both of these agencies routinely review IRB procedures, decisions and records to ensure compliance with regulations and interpretative guidance. Although guidances are not regulations, institutions that fail to comply with them might receive a warning letter or a more severe reprimand, such as an order to temporarily suspend human subjects research (Emanuel et al 2004). The threat of sanctions from federal agencies has encouraged IRBs to interpret regulations more strictly over time (Oakes 2002).

Fourth, the ethical consensus concerning acceptable conduct of research may shift as a result of bioethics scholarship, lawsuits, scandals or controversies, and professional and public debate. Consequently, studies that were regarded as acceptable at one time may no longer be acceptable. For example, from the 1950s to the 1990s investigators frequently conducted research on tissue left over from medical procedures without the patient’s consent (Weir and Olick 2004). For example, in 1951, clinical researchers at Johns Hopkins University derived HeLa, a famous cell line used around the world, from Henrietta Lacks’ cancerous tissue, without her permission (Skloot 2010). Although the regulations allow investigators to conduct research without consent on samples or tissues that have been stripped of personal identifiers, many members of the public and scholars have objected to this practice. An important legal ruling, Moore vs. Regents of the University of California (1990), held that physicians must inform patients if they have any commercial interests
related to using their leftover tissues. Today, most clinical investigators obtain consent from patients before using their leftover tissue in research (Weir and Olick 2004).

Some amount of inconsistency in IRB decision-making is unavoidable and desirable (Edwards et al 2004) because IRBs are likely to interpret regulations and guidelines differently as a result of their members’ differing backgrounds and the local context. While it might be possible to promote greater consistency in IRB review by reducing member diversity, this would not be desirable, because diversity is a strength, not a weakness (Moreno 1995). To make well-reasoned decisions concerning research review, it is important for IRBs to consider different perspectives and opinions, which can be obtained by including members with different backgrounds and concerns. Indeed, research regulations require that IRBs have members from different backgrounds, including scientific, non-scientific, institutional and outside members (Department of Health and Human Services 2009).

Some amount of perceived inconsistency may also be unavoidable because regulations, policies and interpretative guidance sometimes change, and investigators may view IRB decisions as inconsistent even though cases are being treated differently only because the rules and standards have changed.

Dealing with Concerns about Inconsistency

If some amount of real or perceived inconsistency is unavoidable, how should IRBs deal with investigators’ concerns about consistency? First, inconsistencies resulting from lack of knowledge of research regulations or guidelines (and their application) should be avoided (Edwards et al 2004). IRB members should familiarize themselves with relevant regulations and guidelines, and they should keep up with changes in rules and standards. Institutions can help IRB members improve their understanding of the rules and standards by supporting educational programs, such as conferences, lectures and workshops.

Second, IRBs should develop standard operating procedures (SOPs) for research review and oversight. SOPs should cover all aspects of human research protections at the institution, such as regulatory compliance, IRB quorum and voting, record-keeping, communication with investigators, informed consent, protection of vulnerable populations, payments to research subjects, and benefit/risk assessment. SOPs can provide guidance for interpreting regulations and also address areas not covered by regulations. SOPs can help promote consistency by ensuring that research oversight is systematic, principled and thorough.

Third, institutions that conduct, review or support human subjects research should pursue accreditation from the Association for the Accreditation of Human Research Protections Programs (AAHRPP). To receive or maintain AAHRPP accreditation, institutions must comply with standards pertaining to SOPs, education and training, record-keeping, and reporting of adverse events and other aspects of human subjects research (Association for the Accreditation of Human Research Protections Programs 2014a). More than 60% of research-intensive universities in the US have received AAHRPP accreditation or are applying for it (Association for the Accreditation of Human Research Protections Programs 2014b).

Fourth, to dispel perceived inconsistency, IRBs should explain the reasoning behind their decisions. They should set forth the relevant regulations and guidelines that apply to decisions, the IRB’s interpretation of those regulations and guidelines, the information and options that were considered in the decision, and the IRB’s concerns. Investigators should be allowed to ask the IRB to clarify its rulings and to ask the IRB to reconsider its decisions. Transparency helps prevent investigators from feeling like they are being treated unfairly (Martinson et al 2006, 2010).
Fifth, IRBs should maintain and reference a database of past decisions so they can refine their review process over time and not reinvent the wheel when reviewing similar studies. The database should describe the study, the IRB decision(s), and the reason(s) for the decision(s). IRBs should periodically review their decisions for similar studies to identify common characteristics and distinguishing features. They should also take steps to reduce inconsistencies that they discover when reviewing past cases. For example, they could develop an SOP to handle certain types of cases that have been handled inconsistently. IRBs can make the database available to investigators who are preparing IRB submissions, so they can be aware of the issues that are likely to arise during review and they can be assured that their submission will be handled fairly.

Sixth, since numerous studies have shown multiple IRB review increases the risk of inconsistency (Abbott and Grady 2011), institutions should take steps to reduce redundant IRB review in multisite research. Some strategies for reducing the number of IRBs reviewing a multisite study include implementing reliance agreements between institutions concerning IRB review, using central IRBs, and engaging in collaborative review among IRBs (Resnik 2012).

Finally, some have suggested that government agencies should harmonize their regulations (Emanuel and Menikoff 2011). There are significant differences between regulations issued by the DHHS, FDA, Department of Education (DEA), and Environmental Protection Agency (EPA) (Emanuel et al 2004, Resnik 2007). As a result, two studies that are virtually the same may be evaluated differently because different regulations may apply. For example, DHHS regulations include special protections for prisoners, pregnant women and fetuses, but FDA regulations do not (Department of Health and Human Services 2009, Food and Drug Administration 2014a). EPA regulations prohibit any EPA-funded research that intentionally exposes children or pregnant women to drugs or environmental agents, whereas DHHS regulations do not (Department of Health and Human Services 2009, Environmental Protection Agency 2014). Harmonization of regulations may be difficult to achieve, because different federal agencies deal with different issues and face different political pressures from constituencies, but some have argued that it still should be sought (Emanuel and Menikoff 2011).

Nineteenth-century American philosopher and writer Ralph Waldo Emerson (1841) once said, “A foolish consistency is the hobgoblin of little minds, adored by little statesmen and philosophers and divines.” It may be the case that “a foolish inconsistency” has no redeeming value, but consistency in IRB review and oversight is far from foolish. Consistency helps to ensure that human research subjects and investigators are treated ethically and fairly. IRBs should strive for consistency in their decisions, policies and actions.

References


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