



The Role of the Institutional Review Board in Research Oversight: Information for Research Teams to Support Diverse Research Participation

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INTRODUCTION

The COVID-19 pandemic has pushed clinical research into the public limelight. While the COVID-19 clinical trials have made some efforts to enroll a diverse population, Black and Indigenous People of Color (BIPOC) are still dramatically underrepresented.¹ Clinical care and public health policies are shaped by the outcomes of clinical research studies, making this an opportune time to understand the role of Institutional Review Boards (IRBs) in clinical research. IRBs play a critical role in the oversight of clinical research. The essential role of the IRB is to protect the rights and welfare of human research participants – those who agree to participate in the testing of new therapies to help determine whether they are safe and effective. Talking to potential research participants from under-represented communities about the current structure of research oversight and the role of bodies such as the IRB may help to provide reassurance that unethical research practices in the past can't happen today, and may increase willingness to participate in clinical trials.

Historical & Structural Barriers to Diversifying Clinical Trials

While inequality in the US healthcare system is a long-standing issue, the COVID-19 pandemic has exposed the effects of racism and subsequent health disparities that disproportionately impact (BIPOC). Black people are 3.5 times more likely to die from COVID-19 than white people,² and Latino people are nearly twice as likely to die of the

virus as white people. While some of this disparity may be attributed to biomedical factors, "...[l]ong-standing systemic health and social inequities have put many people from racial and ethnic minority groups at increased risk of dying from COVID-19."³ The effects of health inequity are not limited to COVID-19 infection; they permeate nearly every corner of healthcare and clinical research. For example, infant mortality rates are more than twice as high for BIPOC when compared to other racial-

ethnic groups.⁴ Maternal mortality statistics mirror that of infants, with BIPOC women being two to three times more likely to die from pregnancy related causes than White women.⁵ In the context of hereditary cancer syndromes, BIPOC receive less preventative screening, go on to be diagnosed at an advanced stage with fewer treatment options more often than their White counterparts, and have poorer outcomes in general.⁶

The structural racism embedded in the health care system is not a recent phenomenon; it is rooted in historical atrocities that were conducted in the name of science and medicine with no regard for the humans that were unwitting research participants. For example, in 1970 Planned Parenthood of San Antonio conducted a contraceptive study among lower income Hispanic women. This was a double-blind clinical trial designed to study the side effects of an oral contraceptive. The researchers did not disclose to any of the female subjects that they may be given a placebo instead of real contraceptives. Midway through the study they switched the control groups. Out of the 76 participants in the study, ten became pregnant while on placebo, and one became pregnant on the actual birth control.⁷ Another example is the USPHS Syphilis Study at Tuskegee conducted by the U.S. Public Health Service. When the study began in 1932, the researchers promised free medical care, meals, and burial insurance to 600 Black men who were mostly poor sharecroppers in exchange for study

participation. The original goal of the research was to record the natural history of syphilis to support funding requests for treatment programs with the largely ineffective therapies available at the time. However, in the early 1940's, penicillin, which was very effective, became widely available. In order to continue the study, this treatment was withheld from the study participants although many were progressing to advanced syphilis, transmitting the infection to family members, and dying. The study continued until 1972.^{8,9}

Unethical conduct of this nature has had a ripple effect, contributing to generational medical mistrust. This mistrust extends to the clinical trial setting, which influences participant representation. The medical mistrust that drives BIPOC away from research also results in clinical trials where BIPOC are under-represented and gives research results that may not be accessible or appropriate to BIPOC, further widening health disparities.

The Importance of Diversifying Clinical Trials

These historical examples helped plant seeds of generational trauma in BIPOC communities and generational mistrust of the health care system and clinical research in communities of color. If there is no confidence that the health care system will care for people when they need it, it is reasonable to conclude that one cannot expect a person to trust a researcher with their life when it comes to experimental



medications. Evidence of the barriers and facilitators to research participation indicates that subject trust in research is one of the most significant factors associated with willingness to participate in research.¹⁰

The importance of diversifying clinical trials is rooted in the ethical principle of justice. As stated in the Belmont Report, the foundational document for research ethics in the United States; “Who ought to receive the benefits of research and bear its burdens? This is the question of justice, in the sense of ‘fairness in distribution’ or ‘what is deserved’.”¹¹ It is important to ensure that a drug is studied in a population that is likely to use the drug if it is approved.¹² To generate generalizable results,

the participants in research studies must be truly representative of the general patient population.

Ethical Oversight and Protection of Participants’ Rights and Welfare

Today, clinical research is tightly regulated through the collaboration of multiple parties. These regulatory and organizational bodies work together to enforce a series of checks and balances, overseeing the rights, and welfare of research participants. These safeguards start with the Office for Human Research Protections (OHRP) and the US Department of Health and Human Services (HHS). OHRP provides leadership and guidance

for the protection of the rights and welfare of people participating in research, enforcing relevant HHS regulations. These regulations require any organization conducting regulated research on human participants to do so while maintaining a framework laid out by the Belmont Report, safeguarding the rights and welfare of human participants, as outlined in Revised Common Rule 46.101(a) and 46.103(a)). Under these regulations, investigators and institutions are required to report any unanticipated problems or other issues that may arise over the course of the research study. In the case of drug or device studies that are being conducted to support eventual marketing applications, the Food and Drug Administration (FDA) also plays a role in monitoring participant safety.

The Role of the Institutional Review Board

The duty to protect participants falls on all those who conduct human research. In the United States, Congress signed the 1974 National Research Act that established a requirement for IRB review of research supported by the Department of Health, Education and Welfare.¹³ This requirement added a layer of protection for the safety and welfare of research participants by requiring that research protocols meet ethical standards. Since then, IRBs have become known in the research industry for their diligence in applying human research regulations and being well-versed in ethical issues that arise

while research is conducted. Most research is regulated under the FDA and the HHS. Under the regulatory regimes administered by these agencies, IRB review is required for research involving human participants.¹⁴ While the IRB cannot ensure a participant's safety in a clinical trial, its oversight provides a safeguard for participants who decide to participate in human research.

These safeguards are echoed through the IRB's purpose, as well as in its requirements for membership and research review. The regulations require at least five members with varying backgrounds and diversity.¹⁵ When considering diversity, the regulations require that the IRB consider having members on the Board that represent different races, genders, cultural backgrounds, as well as having members of the Board who are sensitive to issues such as community attitudes in an effort to promote respect for its advice and counsel in safeguarding the rights and welfare of human research participants.¹⁶ Additionally, each IRB must have at least one member whose primary concerns are in scientific areas, and at least one member whose primary concerns are in nonscientific areas.¹⁷ To maintain impartiality, the regulations also require at least one member who is not affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution. The regulations prohibit those who have conflicts of interest from voting or participating in initial or continuing review of any project.

In addition to the regulations aiming to create a sense of diversity and impartiality within the IRB, the regulations also establish the criteria needed for research to be approved. Under these criteria, the research must ensure that:

1. The risks to participants are minimized;
2. The risks are reasonable in relation to the anticipated benefits (to the participant and/or to scientific knowledge);
3. There is equitable selection when recruiting participants to a clinical trial;
4. Informed consent and its documentation must be sought by each participant unless an exception applies;
5. There must be a plan for the ongoing monitoring of data;
6. Confidentiality and privacy of participants must be maintained; and
7. Additional safeguards must be in place when involving vulnerable populations such as children, individuals with impaired decision-making capacity, pregnant women, prisoners, and economically or educationally disadvantaged individuals.

(Note: Paraphrased from the full regulatory criteria¹⁸)

Once the research is approved based on meeting the criteria for approval, the regulations require the IRB to review any changes in the research. IRBs are also

required to conduct continuing review at least annually to ensure that the research continues to meet the criteria for approval.¹⁹ Furthermore, if there is a safety issue or the research has harmed a participant, the IRB reviews the problem to determine if serious non-compliance or an unanticipated problem has occurred, whether modification need to be made to the protocol to protect the safety of other participants, and whether the informed consent process should include the new information.

Conclusion

Diversifying clinical trials is key to providing better access to care and improving health outcomes in communities of color. The Centers for Disease Control and Prevention director, Dr. Rochelle P. Walensky stated, "Racism is not just the discrimination against one group based on the color of their skin or their race or ethnicity, but the structural barriers that impact racial and ethnic groups differently to influence where a person lives, where they work, where their children play, and where they gather in community."²⁰ By acknowledging the historical misconduct and the systemic racism that exists in the health care system today, researchers can begin to take steps to rebuild trust that has been broken for many generations. Rebuilding the trust starts with listening to what BIPOC communities need from the health care system and explaining the oversight in place designed to safeguard their rights and welfare in a research setting.

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¹⁴ Office for Human Research Protections. What Regulations Protect Research Participants? 28 Jan. 2020.

¹⁴ 21 CFR §56.107 (2020)

¹⁵ 21 CFR §56.107 (2020)

¹⁶ 45 CFR §46.107 (2018)

¹⁷ Paraphrased from the full regulatory criteria, which are available at <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html#46.111>;

¹⁸ 45 CFR §46.111 (2018); The Food and Drug Administration. Guidance for IRBs, Clinical Investigators, and Sponsors: IRB Continuing Review after Clinical Investigation Approval. Feb. 2012.

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