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Institutional Review Board Liability for Adverse Outcomes

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In 1998, the U.S. Department of Health and Human Services, Office of Inspector General placed institutional review boards (IRBs) under the spotlight. In its examination of clinical trials, the inspector general reported that IRBs, charged with approving all federally funded research, demonstrated a clear lack of cogent oversight, which raised safety concerns for the subjects [1]. In early 2009, the Office for Human Research Protections released a list of various IRB deficiencies—further highlighting their continuing and pervasive problems [2]. Often times, IRBs must cope with pressures from hospitals or universities to grow revenues from research and development, which, in turn, causes the IRB to accept greater liability for adverse clinical-trial outcomes in return for increased monetary compensation. Simply put, today's IRBs face a multitude of issues from different directions. To better understand these issues, it is important to take a look at the history and significance of IRBs.

Background

Throughout history, people have heinously violated human rights and human dignity in the name of biomedical research. The Nazi doctors' experiments during World War II and the infamous Tuskegee Syphilis Study conducted by the U.S. Public Health Service represent the most well-known abuses in modern history. The Nazi experiments ultimately resulted in the torture and death of thousands of unwilling human subjects. These atrocities led to the development of the Nuremburg Code in 1947, which declared the overriding and guiding principle required for any clinical research—informed consent.

The Tuskegee Syphilis Study, which began in 1932, involved approximately 400 African American men infected with syphilis. The U.S. Public Health Service tracked these men for roughly 40 years without providing them with any information or treatment for the disease. As a result, hundreds of them and their families lost their lives to the scourge of a treatable disease. Congress responded with the National Research Act in 1974, which created the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research [3]. In 1979, this commission published the Belmont Report to identify the minimum ethical principles required for human-subject research [4].

The federal government did not stop with the Belmont Report. In 1991, the U.S. Department of Health and Human Services published the Common Rule, which mandated that IRBs approve any federally funded biomedical research in which the

federal government plays a significant regulatory role [5]. IRBs had been around since 1966 when they were created by the U.S. Public Health Service. But the Common Rule standardized their membership, operations, and record-keeping requirements [6]. Specifically, it said that IRBs must consist of at least five members who have diverse backgrounds and levels of experience, including both scientific and nonscientific qualifications. This diversity promotes well-rounded perspectives for review of study protocols and affected populations [7]. Most importantly, the Common Rule required that an IRB must include sufficiently knowledgeable and experienced members to protect the subjects from exploitation during the research process [7].

Overview of the IRB Role

IRBs must verify that new and ongoing research protocols comport with federal criteria ensuring human-subject protection [8]. Typically, an IRB serves a university or hospital, and membership is purely voluntary. Those that join an IRB assume great legal and ethical obligations to ensure the health, safety, and welfare of the human-research subjects. Specifically, an IRB must devise a risk-benefit ratio to determine whether the benefit of the research outweighs the risk to the subject [9]. The government charges IRBs to assess the following: (1) whether a protocol adequately minimizes the risks to study participants and provides for the equitable selection of subjects, (2) the adequacy of the informed-consent documents and procedures, (3) sufficiency of data safety, privacy, confidentiality, and monitoring, and (4) whether the study sufficiently protects vulnerable populations [9]. An IRB reviews and then approves, rejects, or modifies study protocols throughout the biomedical-research process as frequently as necessary to guarantee the safety of the subjects [8]. Failing to adequately insulate subjects from clinical-trial risk may impose liability on culpable IRBs.

Liability Concerns

As the number of clinical trials continues to increase, IRB protocol reviews increase to meet the growing demand. The greater number of protocols under review means greater risk for IRBs that an adverse outcome might occur. IRB members must balance that risk with increased pressure from an IRB member-employer to certify studies and boost cash flow. Hastily approved studies expose investigators, IRBs, and research institutions to significant liability should adverse outcomes occur.

This conundrum is best exemplified by the Jesse Gelsinger case. Jesse, an 18-year-old male with a rare genetic liver disease, enrolled in a phase I clinical trial of gene-therapy treatment conducted at the University of Pennsylvania. A serious, unfavorable reaction to the treatment occurred, and Gelsinger experienced multiple organ failure and died days later. Shortly after his death, new facts surfaced that highlighted significant irregularities in the IRB approval process for the clinical trial. The violations included: (1) a conflict of interest for the primary investigator in terms of pecuniary gain for trial success, (2) failure to report previous adverse events, (3) the enrollment of unqualified subjects, including Gelsinger, and (4) approval of inadequate informed-consent documents and procedures. Luckily for the university,

the plaintiffs did not name any of the IRB members as a party in the litigation, but such errors could have dire consequences for similarly acting IRBs. In particular, a culpable IRB may be subject to multiple types of liability including a breach of confidentiality and a breach of fiduciary duty.

Several high-profile cases brought against IRBs since the early 1970s have settled for undisclosed amounts or failed to reach a decision on the merits of the case [10-12]. An Oklahoma court dismissed *Robertson v. McGee* for lack of subject-matter jurisdiction, but not before the Office for Human Research Protections faulted the IRB for its failure to provide continuous review throughout the clinical-trial process [12]. Ultimately, past litigation signifies that delinquent IRBs can, and will continue to be, joined in litigation for the tort of negligence. This liability may carry severe economic consequences including punitive and consequential damages totaling millions of dollars. If IRBs are found legally negligent and IRB members are named as individuals in the suit, they may possibly have to pay out of their own pockets if ordered by the court or as part of a settlement. The IRB may be joined as part of a hospital or university, in which case, the larger entity would pay. More often than not, when an IRB is implicated, its members are folded as a single body—the IRB—into the suit against to the hospital or university.

Federal regulations delineate legal duties that IRBs must follow. Specifically, they have the responsibility to oversee clinical research, which creates a duty of care or standard of care to protect human subjects from a foreseeable harm that could occur during the course of the study. An IRB that fails to monitor research or halt a study that does not align with federal standards violates its duty of care. Other breaches include approving inadequate informed-consent documents and permitting conflicts of interest on the part of investigators or even IRB members themselves.

Even if these types of breaches occur, an IRB may escape liability if there is no tangible injury to a human subject. In other words, the IRB is not liable for negligence if an injury did not occur. As a reminder, negligence contains four elements: duty, breach of the standard of care, injury, and causation. Based on these elements, a plaintiff can successfully claim negligence against an IRB only by demonstrating that the IRB acted negligently with respect to each element. The degree of injury usually has an impact on the negligence claim, so the graver the injury due to the clinical trial, the easier for the harmed subject to prove negligence against the IRB.

IRBs play a pivotal role in the protection of human subjects participating in biomedical research. This role has its origins in both a checkered history of human research as well as federal regulations designed to prevent atrocious incidences from recurring. Unfortunately, as both the Office of Inspector General and the Office for Human Research Protections reported, despite this critical role and the severe consequences that may result from failed implementation, IRBs routinely fail to provide adequate oversight of biomedical research [2]. As the number of clinical

trials and IRB reviews increase, IRBs will continue to expose themselves to liability should human subjects experience adverse outcomes.

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