CHEST

Institutional Review Boards
Purpose and Challenges

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Institutional review boards (IRBs) or research ethics committees provide a core protection for human research participants through advance and periodic independent review of the ethical acceptability of proposals for human research. IRBs were codified in US regulation just over three decades ago and are widely required by law or regulation in jurisdictions globally. Since the inception of IRBs, the research landscape has grown and evolved, as has the system of IRB review and oversight. Evidence of inconsistencies in IRB review and in application of federal regulations has fueled dissatisfaction with the IRB system. Some complain that IRB review is time-consuming and burdensome without clear evidence of effectiveness at protecting human subjects. Multiple proposals have been offered to reform or update the current IRB system, and many alternative models are currently being tried. Current focus on centralizing and sharing reviews requires more attention and evidence. Proposed changes to the US federal regulations may bring more changes. Data and resourcefulness are needed to further develop and test review and oversight models that provide adequate and respectful protections of participant rights and welfare and that are appropriate, efficient, and adaptable for current and future research.

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ABBREVIATIONS: DHHS = Department of Health and Human Services; FDA = US Food and Drug Administration; IRB = institutional review board; NIH = National Institutes of Health; OHRP = Office of Human Research Protections

Institutional review boards (IRBs) or equivalent bodies provide a core protection for human participants in biomedical and behavioral research in the United States and > 80 other countries around the world.[1] IRBs are charged with providing an independent evaluation that proposed research is ethically acceptable, checking clinical investigators' potential biases, and evaluating compliance with regulations and laws designed to protect human subjects.

Independent review of clinical research by an IRB is required for US studies funded by the Department of Health and Human Services (DHHS) and other US federal agencies, as well as for research testing interventions—such as drugs, biologics, and devices—that are under the jurisdiction of the US Food and Drug Administration (FDA) (Table 1[2,3]). US research institutions can and often do extend federal regulatory requirements to all of their human subjects research. Research conducted outside of the

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TABLE 1] Selected US Regulatory Requirements for IRBs (Paraphrased)

Regulation	Requirements
Membership (45CFR.46 107; 21CFR.56.107)	At least 5 members of varying backgrounds, both sexes, and >1 profession
	At least 1 scientific member, 1 nonscientific member, and 1 unaffiliated member
	Members sufficiently qualified through diverse experience and expertise to safeguard subjects' rights and welfare and to evaluate research acceptability related to laws, regulations, institutional commitments, and professional standards
	At least 1 member knowledgeable about any regularly researched vulnerable groups
	Members report and recusal for conflicts of interest
	Ad hoc experts as needed
Functions/operations (45CFR.46 108; 21CFR.56.108)	Follow written procedures for initial and continuing review and for any changes and amendments
	Written procedures for reporting unanticipated problems, risks, and noncompliance
	Quorum of majority at convened meetings. Approval requires majority vote
Review (45CFR.46 109; 21CFR.56.109)	Authority to approve, require modifications of, or disapprove research
	Require informed consent and documentation (or approve a waiver[1])
	Notify investigators in writing
	At least annual continuing review
Criteria for approval (45CFR.46 111; 21CFR.56.111)	IRB should determine that risks are minimized; risks are reasonable in relation to anticipated benefits, if any, and the importance of the expected knowledge; subject selection is equitable and attention to vulnerable populations; informed consent will be sought and documented; adequate provisions for monitoring; adequate provisions to protect confidentiality; additional safeguards for subjects vulnerable to coercion or undue influence
Authority (45CFR.46. 113; 21CFR.56.113)	Institutional officials cannot approve research that is disapproved by the IRB (45CFR.46 only)
	The IRB can suspend or terminate research for serious harm or noncompliance
Records (45CFR.46. 115, 21CFR.56.115)	Records of research proposals, meetings, actions, correspondence, members, and so forth

CFR = Code of Federal Regulations; IRB = institutional review board.

United States but funded by the US government is subject to the same US federal regulations and so requires IRB review or equivalent protections.[4] Research conducted outside of the United States, not under an investigational new drug that submits data to the FDA for a new drug or biologic license application, must comply with Good Clinical Practice guidelines, which include review and approval by an independent review committee and informed consent.[5] Regulations and laws in many other jurisdictions around the world also require review by an independent research ethics committee or IRB.[6] Regulatory bodies in the European Union, Japan, United States, Canada, Australia, and Nordic countries, among others, follow Good Clinical Practice guidelines such as those delineated by the International Conference on Harmonisation, which require approval by an independent ethics committee or IRB.[7] IRBs or research ethics committees, composed of a group of people independent of the specific research, review proposed research plans and related documents before a study can begin and then periodically (usually annually) for the study duration. The goal of IRB review is to assure that the rights and welfare of participating research subjects will be adequately protected in the pursuit of the proposed research study. To be ethically acceptable and comply with regulatory requirements, the IRB determines that risks to subjects are minimized and reasonable in relation to the importance of the knowledge the study is expected to produce, that the process and outcomes of subject selection are fair (including delineated inclusion and exclusion criteria), and that there are adequate plans for obtaining informed consent.

History of IRBs in the United States

Recognizing that review by impartial others might mitigate conflicting differences in the ethical responsibilities of physician-investigators to research subjects from those of physicians to their patients and, thus, help to