RESEARCH ARTICLE

Is institutional review board (IRB) doing its job right? How to assess this

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Abstract

Objective: To audit the performance of the institutional review board at a cancer hospital.

Method: The retrospective study was conducted at the Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan, in 2021, and comprised all records of the institutional review board from 2005 to 2021. The audit was based on a tool created by the Association for the Accreditation of Human Research Protection Programmes, and elements evaluated included terms of reference, membership lists, review records, meeting minutes, institutional research guidelines as well as other relevant policies.

Result: The institutional review board was found to be in 100% compliance with all the elements set forth in the Association for the Accreditation of Human Research Protection Programmes. The institutional review board was found to be an independent body with a diverse membership and the chairman was always an unaffiliated member. It had defined processes in line with relevant laws and guidelines. Review of research studies was devised to promote the ethical conduct of research.

Conclusion: Though a self-assessment, the audit objectively showed that the institutional review board was in cent per cent compliance with the evaluation instrument developed and used by the Association for the Accreditation of Human Research Protection Programmes. Nevertheless, it still needs further discussion as to how high levels of efficiency and performance of institutional review boards ultimately provide a higher degree of protection to human research participants.

Keywords: Ethics, Research, Ethics committees. (JPMA 73: 1416; 2023) **DOI: https://doi.org/10.47391/JPMA.7157**

Submission completion date: 08-09-2022 **- Acceptance date:** 23-02-2023

Introduction

Violations of the basic rights of human research subjects by researchers in their quest for knowledge has been reported in the past.[1,2] In response, ethics and regulatory oversight of human research protection have evolved to the present state based on the principles that have their origin in the Belmont report and the Declaration of Helsinki, which was first developed in 1964 and has undergone several revisions, with the last update coming at the World Medical Association (WMA) General Assembly in October 2013[3,4] Institutional review board (IRB) is an authorised body charged with primary responsibility to protect the rights and wellbeing of human research participants.[5,6]

Despite the fact that both IRBs and researchers recognise and commit to safeguard the human research participants, the tensions between them is not uncommon.[7] Researchers do not deny the duty to protect human research participants, but often fail to appreciate the relevance of IRB and informed consent process. IRB is often accued of hindering research, and, hence, scientific discoveries.[8]

IRBs have been considered complicated, inconsistent, delaying, equivocal, obstructionist, irrational, inconsistent, biased, powerful, increasingly stringent, and to be overstepping their boundaries.[7] Literature shows that research activities have increased in the last few decades significantly, but the capacity of ethical oversight has not proportionately increased in many parts of the world, especially the developing world.[9,10] The capacity of countries to provide appropriate ethical oversight of health-related research with human subjects somewhat shapes the capacity of IRBs in any particular country. Some established threats to IRBs are inadequate training of its members, lack of accreditation culture and national-level comprehensive guidelines, and scarcity of resources, which together affect the functioning of IRBs.[11,12] These lead to various concerns related to performance of IRBs and quality of their review as well as delays associated with research review process, especially in multicentre studies.[13,14] The IRBs are in dire need of and under pressure to demonstrate performance and efficiency objectively to achieve the confidence of the researchers, but it is established that this ability is constrained by the absence of defined standards and agreed upon benchmarks. Some countries, like the United States and the United Kingdom, have national regulations enforcing some form of registration, accreditation or audit by national-level competent authorities, while others lack such capacities.

Association for the Accreditation of Human Research Protection Programmes (AAHRPP) evaluates and provides accreditation to an institution's human research protection

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programme, including its IRB(s) though this accreditation is voluntary.[15] However, limitation of resources and funding impacts the uptake of such voluntary accreditation services.

Initiatives taken to develop validated tools for this purpose continue to date, but there is no no consensus in sight. Many studies have been carried out in which different tools were used to assess the IRBs.[16-18] In addition, diverse initiatives have been taken to assess the performance of IRBs, using self-assessment method. These include tools developed by the Strategic Initiative for Developing Capacity in Ethical Review (SIDCER), the Office for Human Research Protections (OHRP), and the World Health Organisation's Special Programme for Research and Training in Tropical Diseases (TDR-WHO).[19-21] Investigators have attempted to develop their own self-assessment tools based on some of these guidelines.[22,23] These different models have reported to have different objectives, strengths and limitations.

In Pakistan, the advent of IRBs dates back to the time when the first research ethics committee in Pakistan was founded in 1987.[24] The National Bioethics Committee (NBC) was established in 2002-03, appointed as the national-level competent body responsible for upholding the country's ethical standards in all areas of healthcare.[25] IRBs are not yet accredited, inspected, audited or registered by any national-level competent authority, and, as a result, IRBs remain unregulated.[26] To the best of the authors' knowledge, no centralised register exists to list and identify the various IRBs operating in Pakistan. In this situation, the competence of existing IRBs remain a key knowledge gap.

The current study was planned to audit the performance of IRB at a cancer hospital in an urban setting.

Materials and Methods

The retrospective study was conducted at the Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH&RC), Lahore, Pakistan, in 2021, and comprised all records of IRB from 2005 to 2021.

The self-assessment audit was based on a tool created by the AAHRPP[15] and elements evaluated included terms of reference (TORs), membership lists, review records, meeting minutes, institutional research guidelines as well as other relevant policies (Table 1).

Table-1: Self-assessment tool with listing of domains, standards and elements.

S.No.	Domain	Standard	Elements
1.	Organisation	1.1. The organisation has a systematic and comprehensive Human Research Protection Programme that affords protections for all research participants. Individuals within the organisation are knowledgeable bout and follow the policies and procedures of the Human Research Protection Programme.	A. The organisation has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Programme.
			B. The organisation delegates responsibility for the Human Research Protection Programme to an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the programme.
			C. The organisation has and follows written policies and procedures that allow the Institutional Review Board or Ethics Committee to function independently of other organisational entities in protecting research participants.
			D. The organisation has and follows written policies and procedures setting forth the ethical standards and practices of the Human Research Protection Programme. Relevant policies and procedures are made available to sponsors, researchers, research Staff, research participants, and the Institutional Review Board or Ethics Committee, as appropriate
			E. The organisation has an education programme that contributes to the improvement of the qualifications and expertise of individuals responsible for protecting the rights and welfare of research participants
			F. The organisation has and follows written policies and procedures for reviewing the scientific or scholarly validity of a proposed research study. Such procedures are coordinated with the ethics review process.
			G. The organisation has and follows written policies and procedures that identify applicable laws in the localities where it conducts human research, takes them into account in the review and conduct of research, and resolves differences between federal or national law and local laws.
			H. The organisation has and follows written policies and procedures specifically designed to protect the rights and welfare of research participants during an emergency.
		1.2: The organisation ensures that the Human Research Protection Programme has resources sufficient to protect the rights and welfare of research participants for the research activities that the organisation conducts or oversees.	
		1.3: The organisation's transnational research activities are consistent with the ethical principles set forth in its Human Research Protection Programme and meet equivalent levels of participant protection as research conducted in the organisation's principal location while complying with local laws and taking into account cultural context.	

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S.No.	**Domain**	**Standard**	**Elements**
		1-4: The organisation responds to the concerns of research participants.	a. The organisation has and follows written policies and procedures that establish a safe, confidential, and reliable channel for current, prospective, or past research participants or their designated representatives that permits them to discuss problems, concerns, and questions; obtain information; or offer input with an informed individual who is unaffiliated with the specific research protocol or plan.
			b. The organisation conducts activities designed to enhance understanding of human research by participants, prospective participants, or their communities, when appropriate. These activities are evaluated on a regular basis for improvement.
			c. The organisation promotes the involvement of community members, when appropriate, in the design and implementation of research and the dissemination of results.
		I-5: The organisation measures and improves, when necessary, compliance with organisational policies and procedures and applicable laws, regulations, codes, and guidance. The organisation also measures and improves, when necessary, the quality, effectiveness, and efficiency of the Human Research Protection Programme.	A: The organisation conducts audits or surveys or uses other methods to assess compliance with organisational policies and procedures and applicable laws, regulations, codes, and guidance. The organisation makes improvements to increase compliance, when necessary.
			B: The organisation conducts audits or surveys or uses other methods to assess the quality, efficiency, and effectiveness of the Human Research Protection Programme. The organisation identifies strengths and weaknesses of the Human Research Protection Programme and makes improvements, when necessary, to increase the quality, efficiency, and effectiveness of the programme.
			C: The organisation has and follows written policies and procedures so that Researchers and research staff may bring forward to the organisation concerns or suggestions regarding the Human Research Protection Programme, including the ethics review process.
			D: The organisation has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Programme requirements. The organisation works with the Institutional Review Board or Ethics Committee, when appropriate, to ensure that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate.
		I-6: The organisation has and follows written policies and procedures to ensure that research is conducted so that financial conflicts of interest are identified, managed, and minimized or eliminated.	A: The organisation has and follows written policies and procedures to identify, manage, and minimize or eliminate financial conflicts of interest of the organisation that could influence the conduct of the research or the integrity of the Human Research Protection Programme.
			B: The organisation has and follows written policies and procedures to identify, manage, and minimize or eliminate individual financial conflicts of interest of Researchers and research staff that could influence the conduct of the research or the integrity of the Human Research Protection Programme. The organisation works with the Institutional Review Board or Ethics Committee in ensuring that financial conflicts of interest are managed and minimized or eliminated, when appropriate.
		I-7: The organisation has and follows written policies and procedures to ensure that the use of any investigational or unlicensed test article complies with all applicable legal and regulatory requirements.	A: When research involves investigational or unlicensed test articles, the organisation confirms that the test articles have appropriate regulatory approval or meet exemptions for such approval.
			B: The organisation has and follows written policies and procedures to ensure that the handling of investigational or unlicensed test articles conforms to legal and regulatory requirements.
			C. The organisation has and follows written policies and procedures for compliance with legal and regulatory requirements governing emergency use of an investigational or unlicensed test article.
		I-8: The organisation works with public, industry, and private sponsors to apply the requirements of the Human Research Protection Programme to all participants.	A: The organisation has a written agreement with the sponsor that addresses medical care for research participants with a research-related injury, when appropriate.
			B: In studies where sponsors conduct research site monitoring visits or conduct monitoring activities remotely, the organisation has a written agreement with the sponsor that the sponsor promptly reports to the organisation findings that could affect the safety of participants or influence the conduct of the study.
			C: When the sponsor has the responsibility to conduct data and safety monitoring, the organisation has a written agreement with the sponsor that addresses provisions for monitoring the data to ensure the safety of participants and for providing data and safety monitoring reports to the organisation.
			D: Before initiating research, the organisation has a written agreement with the sponsor about plans for disseminating findings from the research and the roles that researchers and sponsors will play in the publication or disclosure of results.
			E: When participant safety could be directly affected by study results after the study has ended, the organisation has a written agreement with the sponsor that the researcher or organisation will be notified of the results in order to consider informing participants.

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S.No.	Domain	Standard	Elements
		I-9: The organisation has written policies and procedures to ensure that, when sharing oversight of research with another organisation, the rights and welfare of research participants are protected.	
2.	Institutional Review Board (IRB) and Ethics Committee (EC)	II-1: The structure and composition of the IRB or EC are appropriate to the amount and nature of the research reviewed and in accordance with requirements of applicable laws, regulations, codes, and guidance.	A: The IRB or EC membership permits appropriate representation at the meeting for the types of research under review, and this is reflected on the IRB or EC roster. The IRB or EC has one or more unaffiliated members; one or more members who represent the general perspective of participants; one or more members who do not have scientific expertise; one or more members who have scientific or scholarly expertise; and, when the IRB or EC regularly reviews research that involves vulnerable participants, one or more members who are knowledgeable about or experienced in working with such participants.
			B: The IRB or EC has qualified leadership (e.g., chair and vice chair) and qualified members and staff. Membership and composition of the IRB or EC are periodically reviewed and adjusted as appropriate.
			C: The organisation has and follows written policies and procedures to separate competing business interests from ethics review functions.
			D: The IRB or EC has and follows written policies and procedures so that members and consultants do not participate in the review of research protocols or plans in which they have a conflict of interest, except to provide information requested by the IRB or EC.
			E: The IRB or EC has and follows written policies and procedures requiring research protocols or plans to be reviewed by individuals with appropriate scientific or scholarly expertise and other expertise or knowledge as required to review the research protocol or plan.
		II-2: The IRB or EC evaluates each research protocol or plan to ensure the protection of participants.	A: The IRB or EC has and follows written policies and procedures for determining when activities are exempt from applicable laws and regulations, when permitted by law or regulation and exercised by the IRB or EC. Such policies and procedures indicate that exemption determinations are not to be made by researchers or others who might have a conflict of interest regarding the studies.
			B: The IRB or EC has and follows written policies and procedures for addressing protection of participants in research that is exempt from applicable laws and regulations. These functions may be delegated to an entity other than the IRB or EC.
			C: The IRB or EC has and follows written policies and procedures to conduct limited IRB or EC review, if such procedure is used.
			D: The IRB or EC has and follows written policies and procedures to conduct meetings by the convened IRB or EC.
			E. The IRB or EC has and follows written policies and procedures to conduct reviews by the convened IRB or EC.
			F. The IRB or EC has and follows written policies and procedures to conduct reviews by an expedited procedure, if such procedure is used.
			G: The IRB or EC has and follows written policies and procedures for addressing unanticipated problems involving risks to participants or others, and for reporting these actions, when appropriate.
			H: The IRB or EC has and follows written policies and procedures for suspending or terminating IRB or EC approval of research, if warranted, and for reporting these actions, when appropriate.
			I. The IRB or EC has and follows policies and procedures for managing multi-site research by defining the responsibilities of participating sites that are relevant to the protection of research participants, such as reporting of unanticipated problems or interim results.
		II-3: The IRB or EC approves each research protocol or plan according to criteria based on applicable laws, regulations, codes, and guidance.	A.: The IRB or EC has and follows written policies and procedures for identifying and analysing risks and identifying measures to minimize such risks. The analysis of risk includes a determination that the risks to participants are reasonable in relation to the potential benefits to participants and to society.
			B: The IRB or EC has and follows written policies and procedures for reviewing the plans for data and safety monitoring, when applicable, and determines that the data and safety monitoring plan provides adequate protection for participants.
			C: The IRB or EC has and follows written policies and procedures to evaluate the equitable selection of participants.
			D: The IRB or EC has and follows written policies and procedures to evaluate the proposed arrangements for protecting the privacy interests of research participants, when appropriate, during their involvement in the research.
			E: The IRB or EC has and follows written policies and procedures to evaluate proposed arrangements for maintaining the confidentiality of identifiable data, when appropriate, preliminary to the research, during the research, and after the conclusion of the research.
			F: The IRB or EC has and follows written policies and procedures to evaluate the consent process and to require that the researcher appropriately document the consent process.

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S.No.	Domain	Standard	Elements
		II-4: The IRB or EC provides additional protections for individuals who are vulnerable to coercion or undue influence and participate in research.	A: The IRB or EC has and follows written policies and procedures for determining the risks to prospective participants who are vulnerable to coercion or undue influence and ensuring that additional protections are provided as required by applicable laws, regulations, codes, and guidance.
			B: The IRB or EC has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question.
			C: The IRB or EC has and follows written policies and procedures for making exceptions to consent requirements for planned emergency research and reviews such exceptions according to applicable laws, regulations, codes, and guidance.
		II-5: The IRB or EC maintains documentation of its activities.	A: The IRB or EC maintains a complete set of materials relevant to the review of the research protocol or plan for a period of time sufficient to comply with legal and regulatory requirements, sponsor requirements, and organisational policies and procedures.
			B: The IRB or EC documents discussions and decisions on research studies and activities in accordance with legal and regulatory requirements, sponsor requirements (if any), and organisational policies and procedures.
3.	Researcher and research staff	III-1: In addition to following applicable laws and regulations, researchers and research staff adhere to ethical principles and standards appropriate for their discipline. In designing and conducting research studies, researchers and research staff have the protection of the rights and welfare of research participants as a primary concern.	A: Researchers and research staff know which of the activities they conduct are overseen by the Human Research Protection Programme, and they seek guidance when appropriate.
			B: Researchers and research staff identify and disclose financial interests according to organisational policies and regulatory requirements and, with the organisation, manage, minimize, or eliminate financial conflicts of interest.
			C: Researchers employ sound study design in accordance with the standards of the discipline. Researchers design studies in a manner that minimizes risks to participants.
			D: Researchers determine that the resources necessary to protect participants are present before conducting each research study.
			E: Researchers and research staff recruit participants in a fair and equitable manner.
			F: Researchers employ consent processes and methods of documentation appropriate to the type of research and the study population, emphasizing the importance of comprehension and voluntary participation to foster informed decision-making by participants.
			G: Researchers and research staff have a process to address participants' concerns, complaints, or requests for information.
		III-2: Researchers meet requirements for conducting research with participants and comply with all applicable laws, regulations, codes, and guidance; the organisation's policies and procedures for protecting research participants; and the IRB's or EC's determinations.	A: Researchers and research staff are qualified by training and experience for their research roles, including knowledge of applicable laws, regulations, codes, and guidance; relevant professional standards; and the organisation's policies and procedures regarding the protection of research participants.
			B: Researchers maintain appropriate oversight of each research study, as well as research staff and trainees, and appropriately delegate research responsibilities and functions.
			C: Researchers and research staff follow the requirements of the research protocol or plan and adhere to the policies and procedures of the organisation and to the requirements or determinations of the IRB or EC.
			D: Researchers and research staff follow reporting requirements during a research study in accordance with applicable laws, regulations, codes, and guidance; the organisation's policies and procedures; and the IRB's or EC's requirements.

AAHARPP standard and its elements are developed in line with the internationally accepted standards, guidelines and regulations, including the Good Clinical Practice (GCP) guidelines, the International Council for Harmonisation (ICH) E6(R2), Integrated addendum to ICH E6 (R1), guidance developed by the US Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS). There are guidelines that organisation should adhere to for each component. These guidelines comply with those set forth by the US government and many other governments across the world for safeguarding the rights of people taking part in clinical trials.[15]

The Clinical Research office in SKMCH&RC holds overarching responsibilities and provides administrative support and facilitates the process of acquiring the needed trainings for institutional researchers. One of its primary functions is to act as the secretariat to IRB, as well as to support researchers in the conduct of research by providing ongoing oversight throughout the research conduct.

The tool used in the current study was organised under three domains: organisation, institutional review board, and the researchers and staff working in the research department.

Sample size calculation was not formally applied for the current audit. For each listed element, description was recoded, indicating how the element is met. A final indication whether an element was met (M) or not met (NM) was noted.

Results

The IRB was found to be in 100% compliance with all the elements set forth in the AAHRPP (Table 2). The IRB is an unbiased entity in charge of critically analysing and approving all clinical research projects in terms of ethics, carried out in the hospital or involving hospitalised patients or data associated with them. The main responsibility of IRB is to protect the human research participants' interest. Written guidelines clearly identify vulnerable populations, such as people who may be vulnerable to coercion or undue influence, like children, convicts, pregnant women, people with mental illnesses, people facing challenges in terms of finance or literacy, and others, such as hospital workers. Written guidelines further mandate that additional safeguards must be in place to protect these vulnerable populations. The IRB focusses its assessment on concepts that are compatible with GCP recommendations and applicable regulatory requirements initially outlined in the Declaration of Helsinki. The institution's Human Research Programme is governed by research guidelines and defines processes and procedures for meeting professional and regulatory requirements related to research. Diverse mechanisms exist to steer the research teams towards responsible conduct of research. Scientific review committee (SRC) evaluates scientific merits prior to IRB review, ensuring that scientifically sound methods are used in research. IRB review ensures that risks to participants are minimised and are reasonable in relation to proposed benefits. The institution gives sufficient information to potential participants about research studies, enabling them to make informed decision about participation, like confidentiality, risks and benefits, mechanisms and channels for further information, IRB, and how to reach IRB with questions or complaints. Leadership support for operations of IRB provides mechanisms for its audit by internal oversight committees as well as external auditors.

Table-2: Findings of the audit.

S.No.	Domain	Standard	Elements	Description on compliance with the element	Met (M)/ Not Met (N)
1.	Organisation	1.1. The organisation has a systematic and comprehensive Human Research Protection Programme that affords protections for all research participants. Individuals within the organisation are knowledgeable bout and follow the policies and procedures of the Human Research Protection Programme.	A. The organisation has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Programme.	The organisation develops, promotes and updates research guidelines (RG), which sets forth the code for responsible and ethical conduct of research which must be followed by researchers in hospital. It details protection of human research participants and clearly mentions all human research activities are oversee by Human Research Protection Programme. Audits, and service evaluations do not constitute Human Subject research.	M
			B. The organisation delegates responsibility for the Human Research Protection Programme to an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the programme.	RG, clearly states the delegation of this responsibility. Clinical Research Office is responsible for Human Research Protection Programme implementation and maintenance.	M
			C. The organisation has and follows written policies and procedures that allow the Institutional Review Board or Ethics Committee (EC) to function independently of other organisational entities in protecting research participants.	RG, states that Institutional Review Board (IRB) is independent committee. This is further ensured by having a chair and co-chair of IRB, who are not affiliated to the organisation.	M

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S.No.	Domain	Standard	Elements	Description on compliance with the element	Met (M)/ Not Met (N)
			D. The organisation has and follows written policies and procedures setting forth the ethical standards and practices of the Human Research Protection Programme. Relevant policies and procedures are made available to sponsors, researchers, research Staff, research participants, and the Institutional Review Board or Ethics Committee, as appropriate	RG sets forth the ethical standards and practices of the Human Research Protection Programme. These are made available on website of organisation, to ensure access by sponsors as well as any other external collaborating team members, Institutional Review Board members, and research participants in addition to organisation dedicated intranet space for policies, laws, and Standard Operating Procedures which are accessible to all researchers, research Staff of the organisation.	M
			E. The organisation has an education programme that contributes to the improvement of the qualifications and expertise of individuals responsible for protecting the rights and welfare of research participants.	The organisation, in line with its long standing commitment to ethical conduct of research, ensures that individuals responsible for protecting the rights and welfare of research participants, improve their qualifications. The organisation has Employee development and training policy which allows diverse internal and external trainings as needed.	M
			F. The organisation has and follows written policies and procedures for reviewing the scientific or scholarly validity of a proposed research study. Such procedures are coordinated with the ethics review process.	The organisation has Scientific Review Committee (SRC) to review scientific validity of research studies. Prior approval by SRC is mandatory step before a research study is presented to Institutional Review Board, for review. A detailed account of SRC is part of RG.	M
			G. The organisation has and follows written policies and procedures that identify applicable laws in the localities where it conducts human research, takes them into account in the review and conduct of research, and resolves differences between federal or national law and local laws.	Local laws and regulations are clearly identified and listed on organisation dedicated intranet space for policies, laws, and Standard Operating Procedures (SOPs). RG are developed in line with relevant national and international laws, regulations and guidelines.	M
			H. The organisation has and follows written policies and procedures specifically designed to protect the rights and welfare of research participants during an emergency	The organisation has and follows written policies and procedures specifically designed to protect the rights and welfare of research participants during an emergency, which are covered in relevant sections of RG and SOPs.	M

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S.No. **Domain**	**Standard**	**Elements**	**Description on compliance with the element**	**Met (M)/ Not Met (N)**
	1.2: The organisation ensures that the Human Research Protection Programme has resources sufficient to protect the rights and welfare of research participants for the research activities that the organisation conducts or oversees.		To ensure sufficient resources, annual budgeting mechanisms are in place.	M
	1.3: The organisation's transnational research activities are consistent with the ethical principles set forth in its Human Research Protection Programme and meet equivalent levels of participant protection as research conducted in the organisation's principal location while complying with local laws and taking into account cultural context.		Review by Institutional Review Board (IRB) ensures that all research meet ethical and cultural standards of all types of research activities.	
	1-4: The organisation responds to the concerns of research participants.	a. The organisation has and follows written policies and procedures that establish a safe, confidential, and reliable channel for current, prospective, or past research participants or their designated representatives that permits them to discuss problems, concerns, and questions; obtain information; or offer input with an informed individual who is unaffiliated with the specific research protocol or plan.	Informed consent documents of all research studies contain information on how they can contact relevant persons with questions related to study, which enables all enrolled participants to establish contact with the study teams as well as they are provided information on how they can contact IRB for any concerns related to their participation or rights. In addition, similar information is provided to all potential participants via diverse channels including website, standees, research pamphlets, patient's booklets.	M
		b. The organisation conducts activities designed to enhance understanding of human research by participants, prospective participants, or their communities, when appropriate. These activities are evaluated on a regular basis for improvement.	To enhance awareness and understanding of all participants including potential participants, information is made available on website, standees, research pamphlets, patient's booklets, which are reviewed by Patients education committee on a regular basis for improvement.	M
		c. The organisation promotes the involvement of community members, when appropriate, in the design and implementation of research and the dissemination of results.	Institutional Review Board has a representation of community members, who are involved in review of design and implementation of research and the dissemination of results, and can make suggestions for modification, as needed.	M

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S.No.	Domain	Standard	Elements	Description on compliance with the element	Met (M)/ Not Met (N)
		I-5: The organisation measures and improves, when necessary, compliance with organisational policies and procedures and applicable laws, regulations, codes, and guidance. The organisation also measures and improves, when necessary, the quality, effectiveness, and efficiency of the Human Research Protection Programme.	A: The organisation conducts audits or surveys or uses other methods to assess compliance with organisational policies and procedures and applicable laws, regulations, codes, and guidance. The organisation makes improvements to increase compliance, when necessary.	The organisation maintains oversight of all research activities via Clinical Research Office to ensure compliance with RG. In addition, organisation is audited extensively to assess the compliance.	M
			B: The organisation conducts audits or surveys or uses other methods to assess the quality, efficiency, and effectiveness of the Human Research Protection Programme. The organisation identifies strengths and weaknesses of the Human Research Protection Programme and makes improvements, when necessary, to increase the quality, efficiency, and effectiveness of the programme.	The organisation is audited extensively and this includes the audit for Research Protection Programme. In addition, organisation conducts gap analysis.	M
			C: The organisation has and follows written policies and procedures so that Researchers and research staff may bring forward to the organisation concerns or suggestions regarding the Human Research Protection Programme, including the ethics review process.	The organisation has diverse policies where staff can bring forward to the organisation concerns or suggestions regarding any aspect including the Human Research Protection Programme, including the ethics review process.	M
			D: The organisation has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Programme requirements. The organisation works with the Institutional Review Board or Ethics Committee, when appropriate, to ensure that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate.	The organisation has following sections in RG Investigator responsibilities and responsible conduct of research Research misconduct These sections contain detailed guidance on responsible conduct of research as well as mechanisms to address any non-compliance.	M

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S.No.	Domain	Standard	Elements	Description on compliance with the element	Met (M)/ Not Met (N)
		I-6: The organisation has and follows written policies and procedures to ensure that research is conducted so that financial conflicts of interest are identified, managed, and minimized or eliminated.	A: The organisation has and follows written policies and procedures to identify, manage, and minimize or eliminate financial conflicts of interest of the organisation that could influence the conduct of the research or the integrity of the Human Research Protection Programme.	RG has detailed section on Conflict of interest management which applies to all researchers, reviewers and chair of review committees.	M
			B: The organisation has and follows written policies and procedures to identify, manage, and minimize or eliminate individual financial conflicts of interest of Researchers and research staff that could influence the conduct of the research or the integrity of the Human Research Protection Programme. The organisation works with the Institutional Review Board or Ethics Committee in ensuring that financial conflicts of interest are managed and minimized or eliminated, when appropriate.	RG has detailed section on Conflict of interest management which applies to all researchers, reviewers and chair of review committees. The organisation works with IRB ensuring all conflicting interests are declared, and managed appropriately.	M
		I-7: The organisation has and follows written policies and procedures to ensure that the use of any investigational or unlicensed test article complies with all applicable legal and regulatory requirements.	A: When research involves investigational or unlicensed test articles, the organisation confirms that the test articles have appropriate regulatory approval or meet exemptions for such approval.	RG defines the process to review research studies involving investigational medicinal products. It requires that regulatory approval status is clearly mentioned.	M
			B: The organisation has and follows written policies and procedures to ensure that the handling of investigational or unlicensed test articles conforms to legal and regulatory requirements.	RG defines the process to review research studies involving investigational medicinal products.	M
			C. The organisation has and follows written policies and procedures for compliance with legal and regulatory requirements governing emergency use of an investigational or unlicensed test article.	RG as well as a section on Investigational medicinal product in Medication management manual defines it clearly.	M

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S.No.	Domain	Standard	Elements	Description on compliance with the element	Met (M)/ Not Met (N)
		I-8: The organisation works with public, industry, and private sponsors to apply the requirements of the Human Research Protection Programme to all participants.	A: The organisation has a written agreement with the sponsor that addresses medical care for research participants with a research-related injury, when appropriate.	The organisation enters into a written agreement with the sponsor of studies that addresses medical care for research participants with a research-related injury	M
			B: In studies where sponsors conduct research site monitoring visits or conduct monitoring activities remotely, the organisation has a written agreement with the sponsor that the sponsor promptly reports to the organisation findings that could affect the safety of participants or influence the conduct of the study.	The organisation enters into a written agreement with the sponsor that entails a detailed monitoring plan and appropriate mechanisms for sharing of monitoring reports.	M
			C: When the sponsor has the responsibility to conduct data and safety monitoring, the organisation has a written agreement with the sponsor that addresses provisions for monitoring the data to ensure the safety of participants and for providing data and safety monitoring reports to the organisation.	The organisation enters into a written agreement with the sponsor that entails plans for data and safety monitoring and appropriate mechanisms for sharing of its reports	M
			D: Before initiating research, the organisation has a written agreement with the sponsor about plans for disseminating findings from the research and the roles that researchers and sponsors will play in the publication or disclosure of results.	The organisation enters into a written agreement with the sponsor that entails publication and dissemination policies for respective research studies.	M
			E: When participant safety could be directly affected by study results after the study has ended, the organisation has a written agreement with the sponsor that the researcher or organisation will be notified of the results in order to consider informing participants.	This provision depends on the nature of the study, and if study warrants this, legal agreements are required to contain relevant clauses.	M

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S.No.	Domain	Standard	Elements	Description on compliance with the element	Met (M)/ Not Met (N)
		I-9: The organisation has written policies and procedures to ensure that, when sharing oversight of research with another organisation, the rights and welfare of research participants are protected.		RG clearly define that all collaborators must undertake to comply with the RG of the organisation and uphold the principles of protection of research participants, confidentiality and research integrity.	M
2.	Institutional Review Board and Ethics Committee	II-1: The structure and composition of the IRB or EC are appropriate to the amount and nature of the research reviewed and in accordance with requirements of applicable laws, regulations, codes, and guidance.	A: The IRB or EC membership permits appropriate representation at the meeting for the types of research under review, and this is reflected on the IRB or EC roster. The IRB or EC has one or more unaffiliated members; one or more members who represent the general perspective of participants; one or more members who do not have scientific expertise; one or more members who have scientific or scholarly expertise; and, when the IRB or EC regularly reviews research that involves vulnerable participants, one or more members who are knowledgeable about or experienced in working with such participants.	IRB terms of reference (TORs) clearly state the requirement for a valid quorum: "IRB must have a representation of at least one person who is not affiliated with the institution, at least one member who has primary interest in biomedical field and at least one person who has primary interest in non-biomedical field"	M
			B: The IRB or EC has qualified leadership (e.g., chair and vice chair) and qualified members and staff. Membership and composition of the IRB or EC are periodically reviewed and adjusted as appropriate.	IRB leadership (chair, co-chair, and secretarial staff) and members are trained and experienced for their jobs. Training includes both formal as well as on job training. It is considered/argued that in the said context of Pakistan, on job training, offers an acceptable mechanism of training.	M
			C: The organisation has and follows written policies and procedures to separate competing business interests from ethics review functions.	The organisation has and follows policies on conflict of interest as well as Governance, leadership and strategy policy, to separate competing business interests from ethics review functions. This is further ensured by having a chair and co-chair of IRB, who are not affiliated by the organisation.	M
			D: The IRB or EC has and follows written policies and procedures so that members and consultants do not participate in the review of research protocols or plans in which they have a conflict of interest, except to provide information requested by the IRB or EC.	Section on Conflict of interest management in RG states clearly that any reviewer with a conflict of interest will not participate in voting or decision making of review process.	M

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S.No.	Domain	Standard	Elements	Description on compliance with the element	Met (M)/ Not Met (N)
			E: The IRB or EC has and follows written policies and procedures requiring research protocols or plans to be reviewed by individuals with appropriate scientific or scholarly expertise and other expertise or knowledge as required to review the research protocol or plan.	TORs of scientific review Committee as well as that of IRB ensures this aspect.	M
		II-2: The IRB or EC evaluates each research protocol or plan to ensure the protection of participants.	A: The IRB or EC has and follows written policies and procedures for determining when activities are exempt from applicable laws and regulations, when permitted by law or regulation and exercised by the IRB or EC. Such policies and procedures indicate that exemption determinations are not to be made by researchers or others who might have a conflict of interest regarding the studies.	TORs of IRB clearly define this.	M
			B: The IRB or EC has and follows written policies and procedures for addressing protection of participants in research that is exempt from applicable laws and regulations. These functions may be delegated to an entity other than the IRB or EC.	TORs of IRB clearly define this.	M
			C: The IRB or EC has and follows written policies and procedures to conduct limited IRB or EC review, if such procedure is used.	TORs of IRB clearly define this.	M
			D: The IRB or EC has and follows written policies and procedures to conduct meetings by the convened IRB or EC.	TORs of IRB clearly define this.	M
			E. The IRB or EC has and follows written policies and procedures to conduct reviews by the convened IRB or EC.		M

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S.No.	Domain	Standard	Elements	Description on compliance with the element	Met (M)/ Not Met (N)
			F. The IRB or EC has and follows written policies and procedures to conduct reviews by an expedited procedure, if such procedure is used.	TORs of IRB and IRB standard operating procedures (SOPs) clearly define this.	M
			G: The IRB or EC has and follows written policies and procedures for addressing unanticipated problems involving risks to participants or others, and for reporting these actions, when appropriate.	TORs of IRB and IRB SOPs clearly define this, and it is followed.	M
			H: The IRB or EC has and follows written policies and procedures for suspending or terminating IRB or EC approval of research, if warranted, and for reporting these actions, when appropriate.	TORs of IRB and IRB SOPs clearly define this, and it is followed.	M
			I. The IRB or EC has and follows policies and procedures for managing multi-site research by defining the responsibilities of participating sites that are relevant to the protection of research participants, such as reporting of unanticipated problems or interim results.	RG clearly define that all collaborators must undertake to comply with the RG of the organisation and uphold the principles of protection of research participants, confidentiality and research integrity.	M
		II-3: The IRB or EC approves each research protocol or plan according to criteria based on applicable laws, regulations, codes, and guidance.	A.: The IRB or EC has and follows written policies and procedures for identifying and analysing risks and identifying measures to minimize such risks. The analysis of risk includes a determination that the risks to participants are reasonable in relation to the potential benefits to participants and to society.	RG clearly define this, and it is followed.	M
			B: The IRB or EC has and follows written policies and procedures for reviewing the plans for data and safety monitoring, when applicable, and determines that the data and safety monitoring plan provides adequate protection for participants.	RG clearly define this, and it is followed.	M

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S.No.	Domain	Standard	Elements	Description on compliance with the element	Met (M)/ Not Met (N)
			C: The IRB or EC has and follows written policies and procedures to evaluate the equitable selection of participants.	RG, and IRB Review criteria clearly define this, and this is followed.	M
			D: The IRB or EC has and follows written policies and procedures to evaluate the proposed arrangements for protecting the privacy interests of research participants, when appropriate, during their involvement in the research.	RG and IRB Review criteria clearly define this, and this is followed.	M
			E: The IRB or EC has and follows written policies and procedures to evaluate proposed arrangements for maintaining the confidentiality of identifiable data, when appropriate, preliminary to the research, during the research, and after the conclusion of the research.	RG and IRB Review criteria clearly define this, and this is followed.	M
			F: The IRB or EC has and follows written policies and procedures to evaluate the consent process and to require that the researcher appropriately document the consent process.	RG and Organisation policy on informed consent clearly define this, and this is followed.	M
		II-4: The IRB or EC provides additional protections for individuals who are vulnerable to coercion or undue influence and participate in research.	A: The IRB or EC has and follows written policies and procedures for determining the risks to prospective participants who are vulnerable to coercion or undue influence and ensuring that additional protections are provided as required by applicable laws, regulations, codes, and guidance.	RG and IRB Review criteria clearly define this, and this is followed.	M
			B: The IRB or EC has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question.	RG and Organisation policy on informed consent clearly define this, and this is followed.	M

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S.No.	Domain	Standard	Elements	Description on compliance with the element	Met (M)/ Not Met (N)
			C: The IRB or EC has and follows written policies and procedures for making exceptions to consent requirements for planned emergency research and reviews such exceptions according to applicable laws, regulations, codes, and guidance.	RG and Organisation policy on informed consent clearly define this, and this is followed.	M
		II-5: The IRB or EC maintains documentation of its activities.	A: The IRB or EC maintains a complete set of materials relevant to the review of the research protocol or plan for a period of time sufficient to comply with legal and regulatory requirements, sponsor requirements, and organisational policies and procedures.	The IRB or EC maintains a complete set of materials relevant to the review of the research protocol or plan for a period of time sufficient to comply with legal and regulatory requirements, sponsor requirements, and organisational policies and procedures. This is governed via RG and Organisation policy on record retention.	M
			B: The IRB or EC documents discussions and decisions on research studies and activities in accordance with legal and regulatory requirements, sponsor requirements (if any), and organisational policies and procedures.	The IRB or EC documents discussions and decisions on research studies and activities in accordance with legal and regulatory requirements, sponsor requirements (if any) and organisational policies and procedures	M
3.	Researcher and research staff	III-1: In addition to following applicable laws and regulations, researchers and research staff adhere to ethical principles and standards appropriate for their discipline. In designing and conducting research studies, researchers and research staff have the protection of the rights and welfare of research participants as a primary concern.	A: Researchers and research staff know which of the activities they conduct are overseen by the Human Research Protection Programme, and they seek guidance when appropriate.	RG provide guidance which of the activities they conduct are overseen by the Human Research Protection Programme, and they do seek further guidance from relevant staff.	M
			B: Researchers and research staff identify and disclose financial interests according to organisational policies and regulatory requirements and, with the organisation, manage, minimize, or eliminate financial conflicts of interest	RG has detailed section on Conflict of interest management which applies to all researchers, reviewers and chair of review committees. The organisation works with IRB ensuring all conflicting interests are declared, and managed appropriately.	M
			C: Researchers employ sound study design in accordance with the standards of the discipline. Researchers design studies in a manner that minimizes risks to participants.	Researchers are provided guidance and suggested modifications to ensure that they employ sound study design in accordance with the standards of the discipline and design studies in a manner that minimizes risks to participants, at the level of Scientific Review Committee and Institutional Review Board review.	M

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S.No.	Domain	Standard	Elements	Description on compliance with the element	Met (M)/ Not Met (N)
			D: Researchers determine that the resources necessary to protect participants are present before conducting each research study.	Researchers are required to identify the resources and must submit this at the time of submission of IRB.	M
			E: Researchers and research staff recruit participants in a fair and equitable manner.	IRB Review criteria prompts the IRB to review this aspect, for each study under review.	M
			F: Researchers employ consent processes and methods of documentation appropriate to the type of research and the study population, emphasizing the importance of comprehension and voluntary participation to foster informed decision-making by participants.	RG as well as organisation policy on informed consent emphasize and propose mechanisms to promote understanding and voluntary participation to foster informed decision-making by participants.	M
			G: Researchers and research staff have a process to address participants' concerns, complaints, or requests for information.	Researchers and research staff are required to define a process to enable prompt contact and address participants' concerns, complaints, or requests for information that should be incorporated within the informed consent document or at times, via participation card, if needed.	M
		III-2: Researchers meet requirements for conducting research with participants and comply with all applicable laws, regulations, codes, and guidance; the organisation's policies and procedures for protecting research participants; and the IRB's or EC's determinations.	A: Researchers and research staff are qualified by training and experience for their research roles, including knowledge of applicable laws, regulations, codes, and guidance; relevant professional standards; and the organisation's policies and procedures regarding the protection of research participants.	This assessment is done at the level of Scientific Review Committee and Institutional Review Board review, and researchers are required to provide sufficient information to enable this assessment.	M
			B: Researchers maintain appropriate oversight of each research study, as well as research staff and trainees, and appropriately delegate research responsibilities and functions.	PI (or supervisor), as appropriate, is responsible to maintain oversight of research, research staff and trainees, and appropriately delegate research responsibilities and functions. This is reflected and recorded in team log and evidence of oversight meetings.	M
			C: Researchers and research staff follow the requirements of the research protocol or plan and adhere to the policies and procedures of the organisation and to the requirements or determinations of the IRB or EC.	Researchers and research staff must follow RG and the principles set out in these, at all times. This is clearly communicated to researchers at the time of issuance of approval of their respective studies. It is monitored via ongoing oversight and progress reports.	M

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S.No.	Domain	Standard	Elements	Description on compliance with the element	Met (M)/ Not Met (N)
			D: Researchers and research staff follow reporting requirements during a research study in accordance with applicable laws, regulations, codes, and guidance; the organisation's policies and procedures; and the IRB's or EC's requirements.	Researchers and research staff must follow RG, which are based on principles set out in Declaration of Helsinki, Good Clinical Practice (GCP) guidelines, as well as national guidelines, laws and regulations.	M

The IRB membership permits appropriate representation of diverse walks of life, including lawyers, educationists, artists and social activists, in addition to physicians. To attain a valid quorum for a convened meeting, the IRB must have a representation of at least one person not affiliated with the institution, at least one member with primary interest in biomedical field, and at least one person with primary interest in non-biomedical field. Additionally, the IRB frequently evaluates research involving vulnerable subjects. This guarantees that at least one member has knowledge of or experience working with such participants. Quorum requirements are clearly mentioned and IRB can proceed with convened meetings only in the presence of valid quorum. Process for review is uniform for all research studies. IRB members get orientation at the time of induction in IRB. Each member votes and declares conflict of interest, and decision is taken by majority vote.

The IRB's chairperson, vice-chair and members are competent in their specialised fields with experience and work in research ethics and association with IRBs. For research ethics training and experience, both formal as well as on job training os considered. It is argued that in the context of Pakistan, where training opportunities remain few, on-job training offers an acceptable mechanism of training. Chair is always an unaffiliated member as an effort to reduce institutional bias in decision-making. IRB membership and composition are periodically reviewed. Conflict of interest policy is in place to ensure that all investigators and reviewers, including chair of review committees, like IRB, will have to disclose conflict of interest in relation to each study under review, including both financial and non-financial conflicts. If a potential conflict exists, further action is needed to manage this conflict of interest which always requires recusal from voting and decision-making. Detailed report of conflict of interest and all actions taken for its management are generated and reviewed by competent authorities. The IRB has the duty to ensure care for all patients, visitors and institutional employees, if these are recruited in any research, because of their connection to SKMCH&RC. All research proposals carried out in SKMCH&RC should secure approval from the IRB before starting any research activity. The IRB performs initial review before the start of research activity; its continuing review is performed at intervals which are considered appropriate for a proposed research, but at least annually. The IRB also reviews any modifications in the previously approved research, unanticipated problems or interim results. Internationally accepted criteria for initial review of research are followed. The IRB evaluates proposed plans for preserving the privacy of research participants as well as assesses proposed plans the privacy of identifiable data before, during and after the research. The IRB mandates that any human research activity will be done after IRB approval and appropriate informed consent. IRB can waive the requirement of informed consent in cases where it has assessed and determined that waiver of informed consent is justified. These requirements apply to all researches irrespective of the sponsor.

Researcher(s), research team(s) and other research staff who plan and carry out research studies are encouraged and made responsible to protect the human subjects. Researchers are provided support for doing research as well as protecting human subjects. Their research activities are assessed via appraisal system which takes into account responsible conduct of research, and compliance to ethical code of conduct for research. As per the requirements of their field, researchers must use sound study design. Review by SRC and IRB requires and ensures that the researchers make their best efforts to reduce the risks of proposed research by using scientifically sound study designs, and by using procedures which are carried out in routine for diagnosis and treatment, where possible. This ensures that research participants are not exposed to unnecessary risks. The IRB review further ensures that researchers and research staff demonstrate equitable selection of research participants, as required under the IRB review criteria. The criteria further mandate that decision to include or exclude any vulnerable groups should be

based on careful scientific and ethical rationale.

Researchers are required to provide sufficiently detailed information to potential research participants in a language that they understand to ensure that participants can make fully informed decisions for research participation, and the IRB reviews participant information sheets in detail as a vital requirement. The IRB assesses that explanation of research is done with a description of research procedures as well as duration is mentioned. Research guidelines (RGs) and institutional policy on informed consent mandate that potential participants must be informed about risks and benefits of research, alternative options, confidentiality issues, and how any adverse events will be managed, and that sufficient information is provided to clarify that participation in research is voluntary and participants have the right to refuse to participate as well as to withdraw their participation at any time without any loss of privileges or any other type of penalty. This is ensured and monitored closely as a key performance indicator (KPI).

Since this happens to be a self-audit, the need of external audit by competent authority remains valid.

Discussion

Lack of well-established tools for benchmarking of IRB limits the ability to assess the performance of IRBs using uniform standards. However, there is growing interest as well as need for this. It can help competent IRBs to claim credibility, while it can offer an objective assessment to encourage development of IRBs, and a basis to conduct a gap analysis on which they can base activities and initiatives to help address the identified gaps. Ethics review in Pakistan is not a subject widely studied, but existing studies have highlighted longstanding inadequacies in the national ethics review system and local IRBs.[27] This highlights the need for IRBs to find a way to benchmark themselves. This need is legitimate by virtue of lack of any other mechanism of registration or accreditation offered by a competent national body.

Similar motivation was evident in another study in which self-assessment of one IRB indicated satisfactory performance.[28]

It can be argued that IRBs with strong structure, processes and performance have taken initiative to claim credibility, which they deserve. This indicates a positive trend in Pakistan, and awareness that IRBs are exploring the ways to benchmark themselves. It also calls for action to develop some mechanisms for assessments of IRBs by national-level competent authority. A uniform assessment mechanism can enable valuable insight of the competencies of IRBs across the countries. It can give clarity about the expected standards for IRBs in terms of structures, processes and outcomes, and bring harmonisation across diverse IRBs that are currently working as per their own structures and processes. This can accelerate strengthening of IRBs across the country.

While IRBs must strive to attain highest standards of performance and competence, they also need to be mindful that protection of human subjects from harm in real terms ian absolute indicator in this regard.

Conclusion

Though a self-assessment, the internal audit objectively showed that the IRB of SKMH&RC is in complete compliance with the evaluation standards developed and used by AAHRPP, and offers an efficient review process and participant protection in research. Nevertheless, it still needs further discussion on how high levels of efficiency and performance of IRBs ultimately provide a higher degree of protection to human research participants.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

1. Beecher HK. Ethics and clinical research. 1966. Bull World Health Organ. 2001; 79:367-72.
2. Beecher HK. Experimentation In Man. J Am Med Assoc. 1959; 169:461-78. doi: 10.1001/jama.1959.73000220003010.
3. Department of Health, Education, and Welfare, The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report. Ethical principles and guidelines for the protection of human subjects of research. J Am Coll Dent. 2014; 81:4-13.
4. World Medical Association. Ethical principles for medical research involving human subjects. Bull World Health Organ. 2001; 79:373-4.
5. PROTECTION OF HUMAN SUBJECTS. [Online] [Cited 2022 June 21]. Available from: URL: https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html.
6. Byerly WG. Working with the institutional review board. Am J Health Syst Pharm. 2009; 66:176-84. doi: 10.2146/ajhp070066.
7. Grady C. Institutional review boards: purpose and challenges. Chest. 2015; 148:1148-55. doi: 10.1378/chest.15-0706.
8. Whitney SN, Schneider CE. A method to estimate the cost in lives of ethics board review of biomedical research. J Intern Med. 2011; 269:396-402. doi: 10.1111/j.1365-2796.2011.02351_2.x.
9. Bhutta ZAJBotWHO. Ethics in international health research: a perspective from the developing world. Bull World Health Organ 2002; 80:114-20.
10. Hyder AA, Wali SA, Khan AN, Teoh NB, Kass NE, Dawson L. Ethical review of health research: a perspective from developing country researchers. J Med Ethics. 2004; 30:68-72. doi: 10.1136/jme.2002.001933.
11. Abdur Rab M, Afzal M, Silverman AAZH. Ethical practices for health

research in the Eastern Mediterranean region of the World Health Organisation: A retrospective data analysis. PLoS One. 2008; 3:e2094. doi: 10.1371/journal.pone.0002094.

12. Kirigia JM, Wambebe C, Baba-Moussa AJBME. Status of national research bioethics committees in the WHO African region. BMC Med Ethics. 2005; 6:1-7. doi: 10.1186/1472-6939-6-10.
13. Christie D, Gabriel G, Dear K. Adverse effects of a multicentre system for ethics approval on the progress of a prospective multicentre trial of cancer treatment: how many patients die waiting? Intern Med J. 2007; 37:680-6. doi: 10.1111/j.1445-5994.2007.01451.x.
14. Hicks SC, James RE, Wong N, Tebbutt NC, Wilson K. A case study evaluation of ethics review systems for multicentre clinical trials. Med J Aust. 2009; 191:280-2. doi: 10.5694/j.1326-5377.2009.tb02786.x.
15. AAHRPP. Evaluation Instrument For Accredation. [Online] [Cited 2022 May 20]. Available from: URL: https://admin.aahrpp.org/Website%20Documents/AAHRPP%20Evaluation%20Instrument%20(2018-05-31)%20published.pdf.
16. Adams P, Kaewkungwal J, Limphattharacharoen C, Prakobtham S, Pengsaa K, Khusmith S. Is your ethics committee efficient? Using "IRB Metrics" as a self-assessment tool for continuous improvement at the Faculty of Tropical Medicine, Mahidol University, Thailand. PloS One. 2014; 9:e113356. doi: 10.1371/journal.pone.0113356.
17. Jafarey AM, Moazam F. "Indigenizing" bioethics: The first center for bioethics in Pakistan. Camb Q Healthcare Ethics. 2010; 19:353-62. doi: 10.1017/S0963180110000137.
18. Moazam F, Jafarey AM. Pakistan and biomedical ethics: Report from a Muslim country. Camb Q Healthcare Ethics. 2005; 14:249-55. doi: 10.1017/s0963180105050346.
19. Strategic Initiative for Developing Capacity in Ethical Review (SIDCER) SIDCER Recognition Programme. [Online] [Cited 2022 December 20]. Available from: URL: https://tdr.who.int/publications/m/item/2005-01-01-strategic-initiative-for-developing-capacity-in-ethical-review.
20. Office for Human Research Protections. Registration of an Institutional Review Board (IRB) 2005. [Online] [Cited 2022 November 23]. Available from: URL: http://www.hhs.gov/ohrp/assurances/
21. World Health Organization. Product Research and Development Team. (2000). Operational guidelines for ethics committees that review biomedical research. World Health Organization. [Online] [Cited 2022 December 13]. Available from: URL: https://apps.who.int/iris/handle/ 10665/66429
22. Sleem H, Abdelhai RAA, Al-Abdallat I, Al-Naif M, Gabr HM, Kehil ET, et al. Development of an accessible self-assessment tool for research ethics committees in developing countries. J Empir Res Hum Res Ethics. 2010; 5:85-98. doi: 10.1525/jer.2010.5.3.85.
23. Tsan MF, Ling B, Feske U, Zickmund S, Stone R, Sonel A, et al. Assessing the quality and performance of institutional review boards: Levels of initial reviews. J Empir Res Hum Res Ethics. 2020; 15:407-14. doi: 10.1177/1556264620956795.
24. Fox RC, Swazey JP. Why we wrote ... Observing bioethics. Clin Ethics. 2008; 3: 155-158. DOI: 10.1258/ce.2008.008023.
25. National Bioethics Committee, Health Research Institute, National Institutes of Health (NIH) [Online] 2004 [Cited 2022 January 03]. Available from: URL: http://nbcpakistan.org.pk/
26. Mukhtar M, Parveen Z. Pakistan needs a powerful ethics and integrity body. Nature. 2008; 451:887. doi: 10.1038/451887b.
27. Jafarey AM, Iqbal SP, Hassan M. Ethical review in Pakistan: the credibility gap. J Pak Med Assoc 2012; 62:1354-7.
28. Ahsin S, Saeed GEN. Self-evaluation of ethical review committees functioning at Foundation University Medical College (FUMC) through structured constitution-practice-outcome (CPO) assessment model.J Pak Med Assoc. 2017; 67:42-8.