

Guidelines for Institutional Review Committees (IRCs) for Health Research in Nepal



NEPAL HEALTH RESEARCH COUNCIL (NHRC)

**Guidelines for Institutional Review Committees (IRCs)
for
Health Research in Nepal**

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Preface

The Nepal Health Research Council (NHRC) would like to work in close collaboration with all agencies (health care facilities, academic and research institutions) involved in health research for the purpose of establishing a common system of institutional review process. Research on human beings has been conducted since the time of the ancient Greeks. However, ethics related to health and biomedical research is a more recent development. In 1995, NHRC published its first document on research ethics, "NHRC's Ethical Guidelines", which was primarily for research proposal reviewers, ethical committee members, health and medical researchers, health professionals and students of health and medical sciences. Since then NHRC has started to deliver one hour lectures on research ethics in most of the research-related training workshops it has conducted.

In 2001, NHRC published the National Ethical Guidelines for Health Research in Nepal. Since then it has organized a series of workshops and consultative meetings on research ethics in Nepal. Similarly, in 2005, there were three publications: Ethical Guidelines for the Care and Use of Animals in Health Research in Nepal, National Guidelines on Clinical Trials with the Use of Pharmaceutical Products, and Guidelines for Institutional Review Committees (IRCs) for Health Research in Nepal. A workshop on ethics in health research, organized by NHRC on March 13-14, 2008, recommended that it had become time to revise the national ethical guidelines published in the year 2001. Consequently, seven members were delegated as a taskforce committee to accomplish this task, and over the period of revision, a series of workshops was held to garner further suggestions for revisions. The revised guideline was disseminated in a workshop on April 26, 2010. By incorporating the valuable suggestions from this workshop, definitive steps were taken to finalize the ethical guidelines, and a section on the Standard Operating Procedure (SOP) was added. The new national ethical document has been named "National Ethical Guidelines for Health Research in Nepal and SOP", and it was published in January 2011. It assists the Ethical Review Board (ERB) of NHRC in achieving its commitment to promote and protect the dignity, rights, safety and wellbeing of all involved in health research in the culture and environment of Nepal.

As NHRC has already revised its national ethical guidelines for health research in Nepal, it is high time to revise the Guidelines for IRCs for Health Research in Nepal. Therefore, nine members (Annex – I) were delegated as a taskforce committee to accomplish this work, and over the period of revision, a series of meetings have been conducted. The revised Guideline for IRCs for Health Research in Nepal was prepared on July 2014. It is the result of several modifications, and incorporates many valuable suggestions provided by the consultative meeting participants (Annex – II). The draft guideline was presented and widely discussed during a two-day consultative meeting held in Kathmandu on 13 and 14 July 2014.

This document is an updated edition of the Guidelines for IRCs for Health Research in Nepal, which will assist the ERB of NHRC by creating new IRCs at health care facilities, academic and research institutions, and will also provide a basic framework for the development of quality and consistency in the ethical review process. The Guidelines for IRC are intended to facilitate and support ethical review in any institution approving and undertaking the health research process in Nepal. Ethical review should always take into consideration the basic principles of ethics, such as dignity/respect of the person, the values of beneficence, justice, etc., without compromising the scientific merit and quality of the health research.

Acknowledgements

The suggestions from the workshops on Networking of National Health Research Institutes and Strengthening the Linkage of Research and Policy Making on 21-23 June 2013 and Strengthening of ERB & IRC Systems and Practices on 25-26 February 2014 identified that it had become time to revise the Guidelines for IRCs for Health Research in Nepal. In particular, some portions of the previous guideline needed amendments to bring it into alignment with the latest National Ethical Guidelines for Health Research in Nepal and SOP. Therefore, the Guidelines for IRCs for Health Research in Nepal has been published, and is intended to contribute to the development of quality and consistency in the ethical review processes within the health care facilities, academic institutions and research institutions that are involved in approving health research proposals.

In this context, we would like to express our sincere thanks and gratitude to all the members of the Taskforce committee: Prof. Dr. Ramesh Kant Adhikari, Prof. Dr. Jeevan Bahadur Sherchand, Associate Prof. Dr. Aarati Shah, Prof. Dr. Rajendra Kumar BC, Mr. Mohan Krishna Shrestha, Mr. Purushottam Dhakal, Ms. Namita Ghimire, and Dr. Krishna Kumar Aryal.

We are grateful to former Chairman Prof. Dharma Kant Bastola, and former Executive Chief Dr. Guna Raj Lohani for all the support and guidance they provided during the revision process.

We extend our profound thanks to all the participants of the consultative meeting for their enthusiastic participation and thoughtful comments which have made this document more relevant and suited to the context of reality. Heartfelt thanks are offered for their hard work and valuable contributions.

We also express our thanks to the Ethical Review, Monitoring & Evaluation (ER, M & E Section) and all staffs of NHRC, Mr. Nirbhay Kumar Sharma, Mr. Subodh Kumar Karna, Dr. Meghanath Dhimal, Mr. Bijay Kumar Jha, Ms. Sabina Bhandari and Mr. David Norrish who have contributed to the revision of this guideline.

Dr. Khem Bahadur Karki
Member - Secretary

Dr. Krishna Prasad Adhikary
Chairman

Abbreviations

AE	Adverse Event
ADR	Adverse Drug Reaction
CIOMS	Council for International Organizations of Medical Sciences
ERB	Ethical Review Board
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GoN	Government of Nepal
NHRC	Nepal Health Research Council
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
ICH	International Conference on Harmonization
IRC	Institutional Review Committee
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
ER M & E	Ethical Review Monitoring & Evaluation

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1. Introduction

The Nepal Health Research Council (NHRC) was established as a result of a commitment by the Government of Nepal (GoN) to promote scientific and ethically sound health-related research in Nepal.

As mandated by the Act establishing the council, NHRC has been initiating and supporting all activities which enhance research capability and culture in the country. One of the main responsibilities of NHRC is to review and approve health-related research proposals. While reviewing these proposals, NHRC has always prioritized the protection of the rights of humans as well as animals involved in research, while promoting scientifically valid research. The Ethical Review Board (ERB) of NHRC cannot possibly review and monitor all research being conducted in the country. Therefore, NHRC has been supporting the establishment of Institutional Review Committees (IRCs) at health care facilities, academic institutions and research institutions. For the proper functioning of such IRCs, in 2005 NHRC developed IRC guidelines through a consultative process. In the course of time, new theories, principles, and postulates have emerged that limit the proper functioning of IRCs. Thus, to address these issues in the previous guidelines, this document has been developed. The development of guidelines for IRCs is a logical approach to promote and strengthen the capacity for review of health-related research.

The Guidelines for IRCs for Health Research in Nepal (2005) provides a basic framework for quality and consistency in the ethical review process to be undertaken by health care facilities, academic institutions and research institutions in Nepal. However, a series of national workshops, particularly Networking of National Health Research Institutes and Strengthening the Linkage of Research and Policy Making, held on 21-23 June 2013, and Strengthening of ERB & IRC Systems and Practices, held on 25-26 February 2014, have highlighted the need to revise the existing Guidelines for IRCs for Health Research in Nepal. Specifically, some sections of the original guideline need amendments to bring them into alignment with the latest National Ethical Guidelines for Health Research in Nepal and Standard Operating Procedure (SOP) (2011).

All health-related research, including surveys and interventional studies, must be reviewed and approved by an IRC prior to commencement.

This guideline is designed to enable IRCs throughout Nepal to develop their own SOPs to suit the administrative structure of their institute. The revised guideline for IRCs for health-related research in Nepal intends to contribute to the development of quality and consistency in the ethical review processes within institutions that are involved in approving health-related research proposals. The anticipated result would be a uniform approach of assessing ethical conformity of health-related research proposals. This guideline lays the foundation for enhancing the quality of health-related research through the best ethical review practice, by ensuring optimum standards are met in the composition of the committee's that review research proposals as well as in the related operational procedures.

2. Objectives

The overall objective of this guideline is to provide a framework for the formation of IRCs, to detail the functional procedures they should follow while reviewing and approving health-research proposals, and to ensure that the provisions of national guidelines published by NHRC are followed whenever a health-related research proposal is reviewed, approved and monitored.

The specific objectives of this guideline are:

- To ensure that all health care facilities, academic institutions and research institutions follow a similar process in the formation of institutional review committees
- To ensure consistency of the ethical review procedures of all IRCs
- To ensure consistency in the supervision and monitoring of health-related research
- To protect the rights of humans and animals involved in research

3. Role of an IRC

The role of an IRC is to safeguard the dignity, rights, safety and well-being of all actual or potential research participants and ensure that animals, if used for research, are treated humanely. The IRC should ensure the full review and evaluation of all ethical aspects of health-related research proposals it receives prior to any research being carried out in field and/or laboratory settings, according to national ethical guidelines prescribed by NHRC. The IRC should provide independent, competent, and timely review of research proposals. The tasks of the IRC should be executed free of bias and influence (political, institutional, professional, market etc).

The IRC has the authority to ask for research protocol modifications, and to enforce and monitor the conduct of research projects. This includes issues of informed consent and right of all research participants (human or animal) and to suspend or stop any health-related research that violates any ethical issues. This type of supervision and monitoring is applicable to those research projects that are approved by the IRC.

4. Establishing a System of Institutional Review Process

Any health institution which undertakes at least 10 health-related researches in a year is eligible to establish an IRC. The following system should be followed by an IRC:

- It should work within the framework of the highest possible ethical and scientific standards in biomedical research.
- It is mandatory that the IRC must be independent, autonomous and multidisciplinary in nature.
- A mechanism must be developed to ensure clear and efficient communication, harmonization of standards, networking, and cooperation between the IRC and ERB of NHRC. An IRC may implement its own procedure to interact with other IRCs regarding matters of common interest as necessary. Such interactions enable IRCs to learn about prior decisions by other IRCs or the ERB of NHRC that may be relevant to proposed research under review.
- As an IRC may review different types of health-related research, it should be familiar with the different methodologies and ethical considerations that apply to each type of proposed research. As such, a clear procedure needs to be established for the effective review of health-related research proposals.
- The IRC should also develop and establish a mechanism to train its members in order to maintain a high ethical and scientific standard.
- The IRC must be supplied with administrative and financial support from the institute.
- The IRC should outline a clear registration process and fee for reviewing a research proposal.

5. Formation of IRC

Composition of IRC

Each health institution shall set up a mechanism for the establishment of an IRC and for the selection of members to the IRC. The IRC should be multidisciplinary and pluralistic. The chief executive officer or head of the institution should not be the member of any IRC. The IRC should have the freedom to work independently and decide on the merits of research-related proposals without interference from within the institutional framework.

The number of members in the committee shall, in general, depend on the number of fields from which they will be drawn. However, a minimum of 7 to a maximum of 15 is suggested, with an attention to gender, age and discipline balance. The committee should include at least one member who is not affiliated with the institution. If any IRC includes a member from NHRC, the member from NHRC should not be a voting member of the IRC.

Persons with expertise in the following disciplines will be eligible for IRC membership:

- Public health/epidemiology/research methodology
- Biomedical/laboratory science
- Clinical science
- Nursing
- Behavioral and social sciences
- Biostatistics
- Pharmacy/Pharmacologist
- Law/ Teaching/ Journalism/ Community Leadership

Appointment of IRC Members

A clear procedure for recruiting potential IRC members should be established. IRC members should be appointed by the institutional authority. The selection process should be transparent. There should not be any conflicts of interest while making appointments. Only the chairperson should be appointed by the head of the institution. Other members including member-secretary, will be appointed by the chairperson. Member composition should include a balance of gender. The initial orientation, training requirements and means of continuing education of IRC members should be specified. Provisions should be made to appoint an expert consultant on an ad-hoc basis to the IRC, but the consultant should not be considered as a voting member of the IRC.

Terms and Conditions of Appointment

Appointments should be made for tenure of three years, with a provision for re-appointment. A rotational system for membership should be considered that allows for continuity, the development and maintenance of expertise within the IRC, and the regular input of fresh ideas and approaches. Institutions should plan in such away that not more than 50% of the members retire at once, in order to facilitate or ensure continuity of the IRC. Procedures for reappointment, resignation, and discontinuation of appointment (such as for non-attendance) should be specified in the respective SOP. Moreover, the duties and responsibilities of the IRC chairperson, member - secretary and members should clearly be stated in the SOP. The IRC members should provide their current curriculum vitae, and sign for acceptance of the appointment.

6. IRC Office

The institution can setup an IRC Office with necessary administrative support. It should clearly designate the Chairperson, Member-Secretary and Members. The list of the name of IRC members should be displayed in front of the IRC office. There should be at least one administrative or clerical support staff provided by the institution for the IRC office otherwise such tasks should be delegated to one of the officers of the institution. Duties & responsibilities of each IRC member should be clearly stated. All working procedures must be in writing; for example, agenda, minutes, notification of decisions, monitoring and supervision etc.

7. Quorum Requirements

The presence of at least 51% members of the total number of IRC members shall be deemed to constitute quorum or the meeting of IRC. At least one female member and one legal or non-affiliated member must be present to make decisions about any proposed research. Invited experts/consultants should not be counted in meeting quorum requirement.

8. Panel of Experts/Consultants

The IRC can prepare a list of potential experts who are capable and interested in reviewing research proposals. These experts/consultants can be specialists in specific diseases, particular health problems/conditions, health systems, health research methodologies, legal or ethical aspects, or members of special interest/minority groups who can provide special expertise to the IRC on proposed research protocols. It is strongly recommended that the IRC should develop terms of reference for all independent consultants.

9. Qualification of IRC Members

All IRC members should hold an appropriate educational degree, trainings and research experience in health-related research processes. These members should be given an initial orientation on basic principles of research ethics and the proposal approval process adopted by the IRC. The conditions of appointment to the IRC should state provisions available for IRC members to receive introductory training in the work of the IRC as well as ongoing opportunities for enhancing their capacity for ethical review.

10. Review Process and Communicating a Decision

The IRC should provide independent, competent and timely reviews of the ethical aspects of research proposals. The IRC may decide upon the reviewer(s) involved for each proposal. Depending on the nature of the research proposal, it may be reviewed by more than one reviewer. A scoring checklist or format needs to be developed and made available to reviewers in order to maintain consistency and objectivity of the review process.

If only a few proposals (two to three) need to be reviewed at a time, it would be advisable for all IRC members to review the full set of including all associated documents. If a large number of proposals need to be reviewed at each meeting, one IRC member (principal reviewer) is to undertake an in-depth review

including all forms, questionnaires etc., and prepare a summary containing essential details for other members to review.

The following ethical issues should be carefully evaluated during the review process:

- Potential risk to participants should reasonably be less than anticipated benefits.
- Selection of participants should be equitable. If the research involves vulnerable populations, additional safeguards should be included in the research protocol to protect the rights of these people.
- Informed consent should be obtained in an appropriate language understandable by the participant. The informed consent should be signed by the participant or a witness. The participant should be allowed to withdraw from the research at any time without explanation.
- There should be adequate provisions to protect the privacy of participants and maintain confidentiality of data.
- The research plan should make adequate provisions for monitoring during data collection to ensure the safety of participants. The mechanism for compensation in case of injury should be well documented.
- The expected duration of research should be specified prior to approval. In case of amendments, prior approval needs to be given before implementation of amended research activities.
- The IRC should receive periodic and final reports from researchers, a copy of which need to be submitted to NHRC's ERB.

Expedited Review: Most projects will require formal review by the full IRC, but there may be some studies that do not pose any ethical problems ("ethically minor" investigations), where there is minimum risk of distress or injury, be it physical or psychological, to the human participants. This includes outbreak studies, assessments of patient information and education. Such projects may not require review by the full committee. Similarly, under exceptional circumstances of urgency (e.g. a patient with some rare or ill understood condition, epidemics, etc.) the Member–Secretary, in consultation with other IRC members, may give expedited approval. However, the Member-Secretary has the duty to report these approvals to the Chairperson of the IRC at the next meeting of the committee. In the case of any confusion, an application should be reviewed by the full committee.

The IRC may also use the expedited review procedure to review minor changes in previously approved research during the period covered by the original approval. In such cases, the reviewer(s) may exercise all authority of the IRC except disapproval of the proposal. Research may only be disapproved following review by the full committee (Appendix I).

Decisions should only be made by a meeting of the IRC that satisfies quorum requirement. All relevant documents must be considered before a decision is made.

Conduct of Meetings: Meetings should be held on a regular basis at a convenient time and place. The frequency of meetings shall depend on the number of applications that need reviewing. The number of agenda items should be reasonable so that sufficient time can be given to each item for proper discussion. Members should have had sufficient time to peruse the applications prior to the meeting. The principal reviewers in particular should have had adequate time to review the applications assigned to them, and to consult with applicants if necessary.

Depending upon the nature of the research proposal, the IRC can invite the applicant to present the proposal to the panel of experts and IRC members. This will help the IRC to understand the proposal better and guide the researcher appropriately. This procedure should be followed if an independent (expert) reviewer is invited to advise on any particular topic. Minutes of IRC meetings should be maintained in a confidential manner in a standard format.

Conflict of Interest: A conflict of interest is present and interferes with the ability to make an objective evaluation when any of the IRC members are investigators/advisors in a research study being reviewed. In such a situation, the member(s) should disclose the conflict of interest and refrain from participating in the review process by leaving the meeting room.

Communicating a Decision: A decision should be communicated in writing to the applicant according to the IRC procedures. The communication of the decision should include, but not be limited to, the following:

- The exact title of the research proposal reviewed
- The name and title of the research applicant
- The name of the site(s) for the research
- The date and place of the decision
- A clear statement of the decision reached
- Any suggestions by the IRC concerning the research

The name and title of the authorized representative of the IRC or the institution involved should include their signature in the letterhead of the correspondence. The date should be mentioned after the signature.

In the case of a conditional decision, any requirements by the IRC, including suggestions for revision, and details of the procedure for having the application re-reviewed should be clearly stated.

In the case of approval of the study, the communication should include: (a) the need to notify the IRC in case of protocol amendments, (b) the need to notify the IRC in the case of amendments to the recruitment of research participants or the informed consent form, (c) the need to report serious and unexpected adverse events related to the conduct of the study, (d) the need to report unforeseen circumstances, the termination of the study and any information the IRC expects to receive in order to perform ongoing monitoring and supervision of the research study, and (e) the final report and any research articles published in scientific journals.

If the proposal is either rejected or recommended for amendment, clearly stated reason(s) should be provided.

All IRCs shall maintain a record of all research protocols received and reviewed including the following:

- Name and responsible institution or organization or group or individual
- Project identification number(s)
- Principal investigator/co-investigator(s)
- Title of the research proposal
- Ethical approval or non-approval or pending or in process, with date
- Approval or non-approval of any changes to the protocol
- The terms and conditions, if any, of approval of any protocol
- Whether approval is by expedited review
- Action to be taken by the IRC to monitor/supervise the research

Exemption from Review: Ethical review may not be required for studies such as quality control, method validation, or medical audit on condition that the results are not made available in a form that identifies the participants. Use of personal medical records without approaching or involving the patients concerned is, in principle, ethically acceptable provided confidentiality and anonymity are preserved. Such studies are entitled for waiver of the requirement for obtaining informed consent.

11. IRC's Role in Supervision and Monitoring of Health-related Research

The IRC and the institution have the responsibility to ensure that the conduct of all health-related research approved by the IRC be monitored and supervised by procedures and/or by using existing appropriate mechanisms within the institution.

The IRC should establish a follow-up procedure for tracking the progress of all research studies for which a positive decision has been made, from the time of the decision until the termination of the research. The communication between the IRC and the researcher should be clearly documented. The frequency and type of monitoring and supervision needs to be determined by the IRC. The IRC needs to monitor the progress of the research to observe whether it has followed the specific approved research proposal.

Review any proposed revision(s) in the original research proposal (if necessary) and approve or disapprove it/them. The IRC shall require that the principal investigator immediately reports anything which might warrant additional ethical approval of the protocol, including:

- Serious or unexpected adverse effects on research participants or communities
- Proposed changes in the protocol
- Unforeseen events that might affect the continual ethical acceptability of the project

During the supervision and monitoring process, the IRC should review the problems (if any) in the implementation of the research proposal and guide the study team to solve them. It is also recommended that the IRC may provide feedback to the study team in the research process, particularly on problems of identification, methodology, data analysis and lacunae identified in the ethical and scientific aspects of the research (if any), and advise on corrective steps to be taken. The IRC may offer advice regarding the soundness of the conclusions reached on the basis of results of the study, and their relevance to the scientific body of knowledge as well as to health services. It may also advise on the dissemination process, application of research findings into practice and their use in further research.

12. Right of Appeal and Complaints

There should be a clear understanding of who bears ultimate responsibility in the event of complaints and/or litigation by dissatisfied clients of the IRC or research participants. Any institution with an IRC shall establish a mechanism for receiving and promptly handling appeals/complaints or concerns of this nature.

The IRC should have the freedom to work independently and be responsible for their decisions. Such decisions should be based on diligent examination of the proposals and the application of approved methodology. Provided there have been no shortcomings in the review process, it would be the parent institution or organizations responsibility to bear the ultimate responsibility in cases of litigation. Suitable indemnity should be provided for IRC members.

A researcher who receives an unfavorable decision by the IRC has the right of appeal. This appeal is initiated by filing a notice of appeal in writing to the head of the institution within thirty (30) days of the date that he/she received notice of the IRC's decision. In such circumstances, the head of the institution may request the IRC to re-review the proposal. The IRC shall notify the researcher of the rehearing, and the researcher shall have the right to appear at the rehearing to defend the research proposal.

Any research participants involved in a research project have the right to raise complaints or concerns directly either to the chairperson of the IRC or head the institution. In case of an appeal to the IRC by a research participant, the IRC should determine the validity of the complaint and notify the principal investigator of its judgment in the matter. The latter will abide by the decision of the IRC.

13. Recording & Reporting / Documentation & Archiving

The following should constitute the recording and reporting procedure:

- Copies should be kept of all research proposals reviewed, scientific evaluations (if any) that accompany proposals, approved sample consent documents, progress reports and other related documents.
- Minutes of meetings.
- Records of continuing review activities.
- Copies of all correspondence between the IRC and researchers
- A list of all members, reviewers and experts, including their contact details.
- Records should be kept for at least 5 years even after completion of the research study. The records shall be accessible for inspection and copying by authorized representatives of relevant institutions.

The following will constitute the documentation and archiving procedure: All documentation and communication of the IRC should be dated, filed and archived according to written procedures. Proper storage space should be provided for this by the parent institution. A statement is required defining the access and retrieval procedure (including authorized persons) for the various documents and files kept in archive.

Documents that should be filed and archived include, but are not limited to:

- The constitution, written SOP of the IRC, and regular (monthly/annual) reports
- The CVs of all IRC members
- A record of all expenses (including allowances and reimbursements) of the IRC
- Agendas of IRC meetings
- The minutes of IRC meetings
- Copies of all research proposal documents
- Copies of all correspondence of the IRC
- A copy of all decisions and advice given by the IRC
- Notification notices of the completion, premature suspension or termination of all research proposals commenced
- The final summary or final report of all research studies approved by the IRC

14. IRC's Relationship with NHRC

IRCs must receive approval from the ERB of NHRC to be established, by paying Rs. 5000 (five thousand only) as a one-time processing fee to the NHRC. The IRC approval should be renewed every three year from ERB of NHRC. At renewal time, the IRC must pay Rs. 1000 (one thousand only) as a renewal processing fee. The processing fee and renewal fee will not be refundable. If the renewal process is not commenced within 6 months of expiry date, the IRC will be notified for termination of approval. An IRC should inform the ERB of NHRC if there are any changes in its composition.

All approved IRCs should display their approval status from the NHRC prominently in their letter pads. Their decisions will not be considered valid without this approval.

IRCs will be supervised, monitored and evaluated by the national ERB at any time.

All IRCs should submit the following information to the NHRC through an annual report:

- List of all the approved research proposals
- Progress report (six monthly) on all health-related research being conducted under the IRC, with the following information included:

- List of IRC members with their brief updated CV
- Number of meetings and dates conducted
- Number of research proposals submitted, number of approved proposals, and number of pending, suspended, terminated or rejected proposals
- Monitoring procedures in place and any problems encountered
- Number of complaints handled and procedures adopted (if any)
- Electronic copy of report of all research project completed within the year.

Note: The IRC failing to submit above mentioned information / documents to NHRC annually shall not be renewed.

All IRCs should forward the following research proposals to NHRC for approval:

- Research proposed at the national or international level
- Externally sponsored/funded research (the term “externally” indicates not only outside of the country but also outside of the particular health care facility or institution)
- Clinical trials involving human and/or animal participants

Note: the above-mentioned proposals are not to be approved by IRCs other than the national ERB of NHRC. The IRC is also not authorised to provide ethical clearance to any research proposals from researchers outside the institution.

Special instructions to IRCs:

- All research proposals approved by the ERB of NHRC do not need further approval or processing fees from any IRC in the country.
- All IRCs may charge certain fees (for the purpose of research promotion or institutional support) for the approval of proposals, but such fees should not exceed the NHRC proposal reviewing fee structure.
- If a researcher desires to transfer biological samples abroad after a project has been approved without provision for sample transfer, the researcher should resubmit an amended research proposal to the ERB of NHRC for approval. This process will only be valid for postgraduate students, not for externally funded research work.

15. Suspension or Discontinuation of Research

When the IRC is confident that circumstances have arisen in which a research project is not being or cannot be conducted in accordance with the approved protocol, and the welfare and rights of research participants are violated or cannot be protected as a result of such circumstances, the IRC may be required to take the following steps:

- Withdraw approval
- Inform the principal investigator of such withdrawal
- Recommend the suspension or discontinuation of the research project or, any necessary steps to be undertaken
- Make sure that research activities are suspended, stopped or discontinued via the process of withdrawal of ethical approval

16. Annexes

Annex – I

Task Force Committee

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17. Appendixes

Appendix – I

Elements of Ethical Review by the IRC

The primary task of the IRC is to review research proposals and their supporting documents, with special attention given to the informed consent process, documentation, and the suitability and feasibility of the protocol. The IRC also needs to take into account prior scientific reviews, if any, and the requirements of applicable laws and regulations. The following are possible issues to be considered during the ethical review process by the IRC:

1. Scientific design and responsible conduct of the study

- 1.1 The appropriateness of the study design in relation to the objectives of the study, the statistical methodology including sample size, and the potential for sound conclusions.
- 1.2 The justification of predictable risks and inconveniences as well as the anticipated benefits for the research participants and the concerned communities.
- 1.3 Criteria for withdrawal at any time by research participants.
- 1.4 Criteria for suspending or terminating the research as a whole.
- 1.5 Provisions for monitoring and supervision of the research.
- 1.6 Provisions for dissemination of the research results through publication and other media.

2. Recruitment of Research Participants

- 2.1 Content of the informed consent form.
- 2.2 The characteristics of the populations from which research participants will be drawn (including gender, age, and economic status). Be aware of any potential vulnerable populations in the study including women, children, the elderly etc.
- 2.3 The process by which initial contact and recruitment is to be conducted.
- 2.4 The way by which full information is to be conveyed to the potential research participants or their representatives.

3. Care and Protection of Research Participants

- 3.1 The suitability of the investigator(s)' qualifications and experience for the proposed study.
- 3.2 Any plans to withdraw or withhold information or standard therapies for the purpose of the research, and justification for such action.
- 3.3 Any medical care to be provided to research participants during and after the course of the research.
- 3.4 The adequacy of medical supervision and psychosocial support for research participants.
- 3.5 Steps to be taken if research participants voluntarily withdraw from the research.
- 3.6 Outline of any plans to make the study product available to the research participants following completion of research.
- 3.7 A description of any financial costs to research participants.
- 3.8 The compensation/reward for research participants (including money, services and/or gifts).
- 3.9 The provisions for compensation/treatment in the case of the injury/disability/death of a research participant attributable to participation in the research.

4. Informed Consent Process

- 4.1 A full description of the process for obtaining informed consent, and detailed identification of person(s) responsible for obtaining the informed consent.
- 4.2 Clear justification for the intention to include in the research participants who cannot provide consent, and a full account of the arrangements for obtaining consent or authorization for the participation of such individuals.
- 4.3 Assurances that research participants will receive information that becomes available during the course of the research relevant to their participation.
- 4.4 The provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of the research project.

5. Community Considerations

- 5.1 The impact and relevance of the research to the local community and concerned communities from which research participants are to be drawn.
- 5.2 The steps taken for consultation with concerned communities regarding the research procedure.
- 5.3 The influence of community on the consent of individuals.
- 5.4 The extent to which the research contributes to capacity building, such as the enhancement of local healthcare, research, and the ability to respond to public health needs.

6. Expedited Review

- 6.1 For expedited review, the IRC should establish
 - 6.1.1 Procedures for the expedited review of research involving minimal risks to participants. These procedures should specify the following:
 - 6.1.2 The nature of the applications, amendments and other considerations that will be eligible for expedited review.
 - 6.1.3 The types of research to which an expedited review procedure is to apply.
 - 6.1.4 The scope of the Member-Secretary's authority.
 - 6.1.5 The delegation of tasks to sub-committees.
 - 6.1.6 The quorum requirement for expedited review.
 - 6.1.7 The status of decisions (e.g. subject to confirmation by the full IRC or not).
 - 6.1.8 The method of reporting and ratifying decisions by the full Committee.
 - 6.2 Research with potential for physical or psychological harm should generally not be considered for expedited review. This includes drug trials, research involving invasive physical procedures and research exploring sensitive personal or cultural issues.

Appendix – II

Declaration of Helsinki**

Recommendations Guiding Physicians in Biomedical Research Involving Human Subjects

Introduction

It is the mission of the physician to safeguard the health of the people. His or her knowledge and conscience are dedicated to the fulfillment of this mission.

The Declaration of Geneva of the World Medical Association binds the physician with the words "The health of my patient will be my first consideration" and the International Code of Medical Ethics declares "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."

The purpose of biomedical research involving human subjects must be to improve diagnostic, therapeutic and prophylactic procedures and the understanding of the aetiology and pathogenesis of disease.

In current medical practice, most diagnostic, therapeutic or prophylactic procedures involve hazards. This applies especially to biomedical research. Medical progress is based on research, which ultimately must rest in part on experimentation involving human subjects.

In the field of biomedical research a fundamental distinction must be recognized between medical research in which the aim is essentially diagnostic or therapeutic for a patient, and medical research, the essential object of which is purely scientific and without implying direct diagnostic or therapeutic value to the person subjected to the research.

Special caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected. Because it is essential that the results of laboratory experiments be applied to human beings to further scientific knowledge and to help suffering humanity, the World Medical Association has prepared the following recommendations as a guide to every physician in biomedical research involving human subjects. They should be kept under review in the future. It must be stressed that the standards as drafted are only a guide to physicians all over the world. Physicians are not relieved from criminal, civil and ethical responsibilities under the laws of their own countries.

I. Basic Principles

1. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.
2. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted for consideration, comment and guidance to a specially appointed committee independent of the investigator and the sponsor, provided that this independent committee is in conformity with the laws and regulations of the country in which the research experiment is performed.
3. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.
4. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.
5. Every biomedical research project involving human subjects should be preceded by careful assessment of predicable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interests of science and society.

6. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
7. Physicians should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Physicians should cease any investigation if the hazards are found to outweigh the potential benefits.
8. In publication of the results of his or her research, the physician is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.
9. In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is a liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The physician should then obtain the subject's freely-given informed consent, preferably in writing.
10. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a physician who is not engaged in the investigation and who is completely independent of this official relationship.
11. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation. Whenever the minor child is in fact able to give consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.
12. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

II. Medical Research Combined with Clinical Care (Clinical Research)

1. In the treatment of the sick person, the physician must be free to use a new diagnostic and therapeutic measure, if in his or her judgment it offers hope of saving life, reestablishing health or alleviating suffering.
2. The potential benefits, hazards and discomfort of a new method should be weighed against the advantage of the best current diagnostic and therapeutic methods.
3. In any medical study, every patient - including those of a control group, if any - should be assured of the best proven diagnostic and therapeutic method.
4. The refusal of the patient to participate in a study must never interfere with the physician-patient relationship.
5. If the physician considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee (1,2).
6. The physician can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

III. Non-therapeutic Biomedical Research involving Human Subjects (Non-clinical Biomedical Research)

1. In the purely scientific application of medical research carried out on a human being, it is the duty of the physician to remain the protector of the life and health of that person on whom biomedical research is being carried out.
2. The subjects should be volunteers - either healthy persons or a patient for whom the experimental design is not related to the patient's illness.
3. The investigator or the investigating team should discontinue the research if in his/her or their judgment it may, if continued, be harmful to the individual.
4. In research on man, the interest of science and society should never take precedence over considerations related to the well-being of the subject.

**Adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964, and amended by the 29th World Medical Assembly, Tokyo, Japan, October 1975, the 35th World Medical Assembly, Venice, Italy, October 1983 and the 41st World Medical Assembly, Hong Kong, September 1989. World Medical Association, Handbook of declarations, Ferney- Voltaire 1992 (unpublished document; available on request from the World Medical Association, 28 avenue des Alpes, 01210 Ferney- Voltaire, France). [Internet address: <http://www.wma.net/>]

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19. Glossary

Adverse Drug Reaction (ADR)

In the pre-approval clinical experience with a new medicinal product or a product's new usages, particularly as the therapeutic dose(s) may not be established, all harmful and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions.

Adverse Event (AE)

Any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

Approval

The affirmative decision of the IRC that the study proposal has been reviewed and may be conducted at the institution site within the constraints set forth by the IRC, the institution, good clinical practice (GCP), good laboratory practice (GLP), and the applicable regulatory requirements.

Benefit: A favorable consequence arising from a study, for example the demonstration that a drug/vaccine is effective in a randomized controlled trial.

Blinding

A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-blinding usually refers to the participant(s) being unaware, and double-blinding usually refers to the participant (s), investigator(s), monitor, and, in some cases, data analyst(s), being unaware of the treatment assignment(s).

Clinical Investigation

Any experiment in which a drug/vaccine is administered, dispensed or otherwise used, involving a required number of research participants. For the purposes of this document, an experiment is any use of a drug/vaccine except for the use of a marketed drug/vaccine in the course of medical practice.

Clinical Trial

A systematic study involving a pharmaceutical product or biomedical device with research participants in order to discover or verify the effects of and/or identify any adverse reaction to investigational products, and/or to study the absorption, distribution, metabolism and excretion of the products with the objective of ascertaining their efficacy and safety. Clinical trials are generally classified into Phases I to IV. It is not possible to draw distinct lines between the phases, and diverging opinions about details and methodology do exist. A brief description of the individual phases, based on their purposes as related to the clinical development of a pharmaceutical product or device, is given below:

Phase I: These are the first trials of a new active ingredient or new formulations or device in human beings, often carried out in healthy volunteers. Their purpose is to establish a preliminary evaluation of safety, and a first outline of the pharmacokinetic and, where possible, a pharmacodynamic profile of the active ingredient in humans, or sensitivity or specificity of a device.

Phase II: These trials are performed in a limited number of human participants and are often of a comparative (e.g. placebo-controlled) design. Their purpose is to demonstrate therapeutic activity and to assess short-term safety of the active ingredient or device in patients suffering from a disease or condition for which the active ingredient or device is intended. This phase also aims at the determination of appropriate dose ranges or regimens or exposure to a device and (if possible) clarification of dose-response or device-response relationships in order to provide an optimal background for the design of extensive therapeutic trials.

Phase III: Trials in larger (and possibly varied) patient groups with the purpose of determining the short and long-term safety/efficacy balance of formulation(s) of the active ingredient, and of assessing its overall and relative therapeutic value. The pattern and profile of any frequent adverse reactions must be investigated and special features of the product or device must be explored (e.g. clinically relevant drug interactions, factors leading to differences in effect such as age). These trials should preferably be of a randomized double-blind design, but other designs may be acceptable, e.g. long-term safety studies. Generally, the conditions under which these trials are carried out should be as close as possible to normal conditions of use.

Phase IV: Studies performed after marketing of the pharmaceutical product or device. Trials in phase IV are carried out on the basis of the product or device characteristics on which the marketing authorization was granted and are normally in the form of post-marketing surveillance, or assessment of therapeutic value or treatment strategies or sensitivity or specificity of a device. Although methods may differ, these studies should use the same scientific and ethical standards as applied in pre-marketing studies.

After a product or device has been placed on the market, clinical trials designed to explore new indications, new methods of administration or new combinations, etc. are normally considered as trials for new pharmaceutical products or devices.

Community

A community is a group of people understood as having a certain identity due to the sharing of common interests or to a shared proximity. A community may be identified as a group of people living in the same village, town, or country and, thus, sharing geographically proximity. A community may be otherwise identified as a group of people sharing a common set of values, a common set of interests, or a common disease.

Comparator Product

A pharmaceutical or other product (which may be a placebo) used as a reference in a clinical trial.

Compensation

That which is given in recompense, as an equivalent rendered, or remuneration.

Compliance

Adherence to all the trial-related requirements, GCP requirements, and the applicable regulatory requirements.

Consent Form

An easily understandable written document that documents a potential participant's consent to be involved in research and which describes the rights of an enrolled research participant. This form should communicate the following in a clear and respectful manner: research time-frame; title of research; researchers involved; purpose of research; description of research; potential harms and benefits; treatment alternatives; statement of confidentiality; information and data to be collected; how long the data will be kept, how it will be stored and who can access it; any conflicts of interest; a statement of the participant's right to withdraw from participation at

any point; and declarative statement of understanding that the potential participant agrees to and signs. The consent form should be in a language that the potential participant understands. For potential participants with limited literacy, the verbal communication of the consent document details should be provided along with proper documentation of consent, if it be given.

Confidentiality

Maintenance of the privacy of research participants including their personal identity and all personal information.

Conflict of Interests

A conflict of interest arises when a member (or members) of the IRC holds interests with respect to specific proposals for review that may jeopardize his/her (their) ability to provide a free and independent evaluation of the research focused on the protection of the research participant. Conflict of interests may arise when an IRC member(s) has financial, material, institutional, or social ties to the research.

Contract

A written, dated, and signed agreement between two or more involved parties that sets out any arrangements regarding delegation and distribution of tasks and obligations and, if appropriate, financial matters. The protocol may serve as the basis of a contract.

Decision

The response given by the IRC to the research proposal following review, which may be either positive or negative.

Direct Access

Permission to examine, analyze, verify, and reproduce any records and reports that are important to evaluation of a clinical trial. Any party (e.g. domestic and foreign regulatory authorities, sponsor's monitors or auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory

requirement(s) to maintain the confidentiality of participants' identities and the sponsor's proprietary information.

Documentation

All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records, and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial/study, the factors affecting a study/trial, and the actions taken.

Ethical Guidelines

Guidance documents which assist with decisions relating to the responsibility to adhere to established and relevant standards of ethical principles and practice.

Expedited Review

Review of proposed research by the IRC Member Secretary or a designated voting member or group of voting members rather than by the entire IRC.

Good Clinical Practice (GCP)

A standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials/study that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial/study participants are protected.

ID

A unique identifier assigned by the investigator to each study/trial participant to protect the participant's identity and used in lieu of the participant's name when the investigator reports adverse events and/or other study/trial-related data.

Informed Consent

A process by which a research participant voluntarily confirms his or her willingness to participate in a particular research project. This consent should only be sought

after all appropriate information has been given about the research project, its objectives, potential benefits, risks and inconveniences, and of the subject's rights and responsibilities in accordance with the current revision of the Declaration of Helsinki (see Appendix 1).

Inspection

The act by a regulatory authority (/ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority (/ies) to be related to the clinical trial/study and that may be located at the site of the trial/study, at the sponsor's and/or contract research organization's facilities, or at other establishments deemed appropriate by the regulatory authority (/ies).

Institution

Any public or private entity or agency or medical or health facility where study/clinical trials are conducted.

Institutional Review Committee (IRC)

An independent body comprised of medical, scientific and non-medical members, whose responsibility is to ensure the protection of the rights, safety, and well-being of human participants participating in a particular research project, and to consider general health research ethics, thereby providing public reassurance. It should be constituted and operated so that its tasks can be executed free from bias and from any influence of those who are conducting health research in the respective institution.

Investigator

A duly qualified member of the respective institution can function as an investigator. He or she should be responsible for the conduct of a research project and for the rights, health and welfare of the research participants. The investigator should have qualifications and competence in accordance with national laws and regulations as evidenced by up-to-date curriculum vitae and other credentials. A person who has

an academic degree in relevant biomedical or health-related subjects and other necessary professional credentials could be an investigator for a research project.

IRC Approval

A decision by the IRC that the proposal has been reviewed and may be conducted at an institution in accordance with the conditions set forth by the IRC.

Minimum Risk

When the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Personal Data

Data that relate to a living person and contain personally identifying information.

Principal Investigator (PI)

The main researcher responsible for the overall execution of a particular research project.

Privacy

The state or condition of being alone, undisturbed, or free from public attention, as a matter of choice or right; seclusion; freedom from interference or intrusion; absence or avoidance of publicity or display; secrecy, concealment, discretion; protection from public knowledge or availability.

Private Information

Information about behavior that occurs in a context when an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for a specific purpose by an individual and which the individual can reasonably expect will not be individually identifiable (i.e., a medical record, questionnaire, etc.).

Protocol

A document which states the background, rationale and objectives of a research project and describes its design, methodology including statistical considerations, and the conditions under which it is to be performed and managed. The protocol should be dated and signed by the investigator. The protocol also refers to protocol amendments.

Protocol Amendments

A written description of change(s) to, or formal clarification of, a protocol.

Quality Assurance (QA)

All those planned and systematic actions that are established to ensure that a study/trial is performed and data generated, documented (recorded), and reported in compliance with GCP and applicable regulatory requirement(s).

Quality Control (QC)

The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the study/trial-related activities have been fulfilled.

Quorum

A quorum is the minimum number of members that must be present to constitute a valid meeting where decisions can be taken concerning submissions put forward for ethical review. A meeting is quorate when a quorum is present.

Raw Data

All records or certified copies of original observations, clinical findings or other activities in a research project. Such material includes laboratory notes, memoranda, calculations and documents, as well as all records of data from automated instruments or exact verified copies in the form of photocopies, microfiches etc. Raw data can also include photographic negatives, microfilm or digital media (e.g. computer CD).

Reimburse

To repay (a sum of money which has been spent or lost).

Regulatory Authorities

Bodies having the power to regulate. This includes the authorities that review submitted study data and those that conduct inspections.

Research

A systematic investigation including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Researcher

A person who engages in the methodical and systematic investigation of any health study with the goal of contributing to new knowledge.

Research Participant

An individual who is or becomes a participant in research, either as a recipient of the test article [investigational product(s)] or as a control. A participant may be either a healthy individual or a patient.

Revision

Requirement by the IRC to alter the protocol in some way prior to approval or additional review by the committee.

Risk

Risks include physical risks (such as the possibility of having an allergic reaction), psychological risks (such as the possibility of emotional distress), social risks (such as the possibility of embarrassment or ridicule by peers), legal risks (such as the possibility of being sued because of information shared with the researcher), and economic risks (such as the possibility of being fired from one's job for sharing information with the researcher). Higher risk-levels are acceptable only when there are greater potential benefits (such as in cancer research).

Serious Adverse Event (SAE)

Any untoward medical occurrence that, at any dose:

- results in death
 - is life-threatening
 - requires inpatient hospitalization or prolongation of existing hospitalization
 - results in persistent or significant disability/incapacity
- or
- is a congenital anomaly/birth defect
 - results in important medical events that may not be immediately life-threatening or cause death or hospitalization, but may jeopardize the patient or may require intervention to prevent the afore mentioned outcomes

Source Data

All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies)

Source Documents

Original documents, data, and records (e.g. hospital records, clinical and office charts, laboratory notes, memoranda, participant's diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm, magnetic media, X-rays, participant files, and records kept at the study laboratories, pharmacies, and medico-technical departments involved in the study.

Sponsor

An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a research study.

Standard Operating Procedure (SOP)

A detailed, written instruction to achieve uniformity of performance of a specific function.

Study Report

A written description of a study of any therapeutic, prophylactic, or diagnostic agent conducted in human participants, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report.

Study Site

The location(s) where study-related activities are conducted.

Supervision and Monitoring

An officially conducted procedure (i.e. review of the conduct of certain research), either by an independent IRC team or jointly with the national ERB (if necessary) at the site of investigation.

Unexpected ADR

An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g. investigator's brochure for an unapproved investigational product or package insert/summary of characteristics of an approved product)

Verification (Validation) of Data

The procedures carried out to ensure that the data contained in the final report match original observations. These procedures may apply to raw data or data in case-report forms (in hard copy or electronic form), computer printouts, statistical analyses and tables.

Voluntary

(1) Performed or done of one's own free will, impulse, or choice; not constrained, prompted, or suggested by another; (2) free of coercion, duress, or undue inducement. Used in the health and disability care and research contexts to refer to a consumer's or participant's decision to receive health or disability care or to participate (or continue to participate) in a research activity.

Vulnerable (Research) Participants

Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests. Individuals whose willingness to volunteer in a research study may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate may also be considered vulnerable. Examples include members of a group with a hierarchical structure, such as medical, pharmacy, dental and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention (e.g. prisoners). Other vulnerable persons include patients with incurable diseases, people in nursing homes, unemployed or impoverished people, patients in emergency situations, ethnic minority groups, homeless people, nomads, refugees, minors, people with physical frailty, mental disability or substance abuse-related disorders, and those incapable of giving consent. This list may not be exhaustive as there may be circumstances in which other groups are considered vulnerable: for example women in an orthodox patriarchal society, pregnant women and children.

Witness

A person who will not be influenced in any way by those who are involved in the research project, who is present and may provide assistance if required when the subject's informed consent is being obtained, and documents that this consent is given freely by signing and dating the informed consent form.



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