RESEARCH PROPOSAL

Department

TITLE

Principal investigator			
E-mail			
Degree	BDS, MPH	College	Avicenna Medical and Dental College
Department	Community and Preventive Dentistry	Mobile	

OTHER INVESTIGATORS

PURPOSE OF STUDY

The purpose of the present study was to assess

RESEARCH BACKGROUND

INTRODUCTION

RATIONALE

LITERATURE REVIEW

AIMS AND OBJECTIVES

MATERIALS AND METHODS

Study design:

Study sample:

Study sampling technique: **Study setting:**

Study population:

Study duration:

Inclusion Criteria:

Exclusion Criteria:

SAMPLE SIZE CALCULATOR

METHODOLOGY

ETHICAL DECLARATION

REFERENCES

Annexure A

Informed Consent Form

باخبر رضامندی فارم

QUESTIONNAIRE


THANK YOU!

AVICENNA MEDICAL COLLEGE AND DENTAL HOSPITAL

INSTITUTIONAL REVIEW BOARD (IRB)

STANDARD OPERATING PROCEDURES (SOPs)

Version 2.0

Revised by: Secretary Institutional Review Board **Date: 07-Mar-2024**

Approved By: _____

Prof. Dr. Gulfreen Waheed (Chairperson IRB/ERC)
Avicenna Medical College and Hospital, Lahore

STANDARD OPERATING PROCEDURES (SOPs)

I. BACKGROUND

The Ethical Mandate to Protect Human Subjects

Research at Avicenna Hospital must be carried out in an ethical manner. The basic ethical principles guiding research involving human subjects are:

a. Respect for persons (applied by obtaining informed consent, consideration of privacy, confidentiality, and additional protections for vulnerable populations)

b. Beneficence (applied by weighing risks and benefits)

c. Justice (applied by the equitable selection of subjects)

(Reference : The Belmont Report)

II. IRB PROCEDURES

A. Process for review and modification of IRB SOPs

1. Procedures for Review, Revision and Approval of Policies and Procedures

a. Changes to regulations, Federal (NBC & DRAP) guidelines, research practices, or local policies and procedures may require a new SOP or revision of a previously issued SOP.

b. Each approved SOP will be reviewed no less than three years from the date of approval as described in this policy. The review date is determined as three years from the last date of approval.

i. The IRB Secretary or designee reviews the SOP and provides the revised policy and procedure to a designated member(s) of the IRB Executive Committee for approval. If the IRB Director or designee determines that significant changes to a policy must be made, the revised policy and procedure may be sent to the IRB committee for discussion.

ii. The review and approval of the SOP is documented by an IRB Secretary or designee who records the policy and procedure, the date approved (e.g. mm/dd/yyyy) and the member(s) responsible for approval. The approval date is the effective date.

2. Procedures for SOP Dissemination and Training

a. When new or revised SOPs are approved, they will be disseminated to the appropriate individuals and departments.

b. Any new or revised policy or procedure or new regulation is disseminated to the IRB members and staff by the IRB secretary or designee. Record of dissemination and any applicable training is documented by the IRB secretary or designee.

III. DEFINITION OF THE PURPOSE & INDEPENDENCE OF THE IRB

The institution established an independent IRB and empowered it to protect the rights and welfare of human research participants. The purpose of the IRB is to review and approve, require modifications in (to secure approval), or disapprove all human research activities in order to assure that the rights and welfare of individuals involved as subjects of research are being protected in accordance with applicable regulations.

IV. AUTHORITY OF THE IRB

A. Scope of Authority Defined

The Chairperson is responsible for ensuring that the IRB functions independently, and that members have direct access to him/her if they experience undue influence or if they have concerns about the IRB. The Chairperson/Vice Chairperson cannot approve a study that has been disapproved by the IRB. IRB fosters institutional culture that supports the ethical conduct of all research. IRB members (including the Chair) should remove themselves from the review of any research in which they or close family members have a conflicting interest.

The Chairperson gives the IRB full authority:

a. to approve, require modifications in to secure approval, and disapprove all research activities overseen and conducted by the organization...
b. to suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects.
c. to observe, or have a third party observe the consent process and the conduct of research

Research Investigators and Study Staff

The **Principal Investigator (PI)** certifies that he/she will conduct the study according to applicable laws, regulation, ethical standards and guidelines governing the protection of human research subjects. The Principal Investigator is required to be qualified by training, and assumes ultimate responsibility and oversight for the protocol to conduct research according to sound research design, assures adequate resources are available, selects and oversees trained study staff and delegates duties prospectively and consistent with Scopes of Practice to research team members, assures that human research training requirements are met, weighs risk benefits for subjects, implements fair recruitment, responds to subject complaints or requests for information, develops an informed consent process, minimizes risk and develops plans to monitor safety and detect harm, reports safety findings and unanticipated problems, discloses conflicts of interest, adheres to IRB Conditions of Approval, national regulations, sponsor and organizational policy in order to conduct the study appropriate to human subject protections. Investigators are required to submit complete protocols and relevant study related materials to the IRB for review, including continuing reviews and status updates as required by the IRB.

Promptly Reporting Changes in Principal Investigator (PI) :this means promptly reporting any changes in the PI to the IRB. Changes in the PI must be reviewed and approved by the IRB prior to the initiation of the change to ensure the new individual meets the criteria for conditions of approval.

B. Regulatory Agencies

The IRB is subject to regulation and inspection by governmental regulatory agencies (*e.g.* DRAP) and sponsor representatives/CROs.

V. MEMBERSHIP OF THE IRB

A. Committee Composition

The IRB has five voting members. Members and alternates are appointed in writing by IRB Chair and members for 3 years and may be re-appointed for 3 year terms. Committee composition is reviewed annually according to the following criteria: (1) professional representation, (2) diversity, (3) institutional knowledge, (4) gender representation, (5) voting status, (6) training and background, (7) potential conflicts of interest, (8) if one member's primary concerns are in scientific areas, (9) if one member's primary concerns are in non-scientific areas, (10) if community members are not associated with Avicenna hospital or are not part of the immediate family of a person who is affiliated with Avicenna (11) if IRB membership is appropriate given the research being reviewed, (12) if membership includes representatives with an interest in or experience with vulnerable populations either as members or ad hoc consultants, (13) if alternate members have appropriate training and backgrounds to serve as replacements, (14) if ad hoc reviewers are utilized when IRB members do not have the expertise necessary to adequately review research, and if (15) the number of IRB meetings and the frequency of meetings are adequate for the number and types of studies.

1. **Chairperson Selections and Appointment**
The Chairperson has expert knowledge in human subject protections. The Chairperson must be a highly regarded and respected leader in order to promote respect for the IRB's advice and counsel throughout Avicenna Hospital and externally.

2. **Length of Term/Service**
The Chairperson is appointed in 3-year increments and may be reappointed for 3 year terms indefinitely.

3. **Duties**
The Chairperson has primary responsibility for conducting Committee business. He/she directs Committee proceedings in accordance with institutional and regulatory requirements. He mentors Committee members, institutional officials, and investigators to ensure that the rights and welfare of research subjects are protected. He/she functions as a role model and conducts business fairly and impartially. He/she is the signatory official for official IRB minutes and official IRB correspondence. He/she may delegate signing authority to Committee members

4. **Removal**
If necessary, the Chairman Abdul Waheed Trust may relieve a Chair or Vice-Chair from the Committee service due to repeated non-attendance, lack of participation in continuing education, or other problematic performance issues. Should this action be required, the Director will notify the Committee members.

B. The IRB Members

a. Each IRB must include at least one voting member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. Members whose training, background, and occupation are within a behavioral or biomedical research discipline should be considered a scientist, while members whose training, background, and occupation are outside of a behavioral or biomedical research discipline should be considered a nonscientist.

b. Each IRB must include at least one voting member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

c. An IRB cannot have a member participate in the IRB's initial or continuing review of any project in which the member has a conflict of interest, except to provide information requested by the IRB.

d. An IRB may invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals are not allowed to be voting members of the IRB.

e. Facility Directors, their administrative staff, other facility senior administrators such as Associate or Assistant Directors or Chief Nurse, and NPC Administrative Staff may observe IRB meetings, but may not serve as members of the facility's IRB.

f. If alternate members are appointed to the facility's IRB, the IRB's written procedures must describe the appointment and function of alternate members, and the IRB membership roster must identify by name the primary member(s) for whom each alternate member may substitute. The alternate members must have similar member qualification(s) of the primary member they replace.

Length of Term/Service

Members serve terms in three-year increments and may be re-appointed. Due to the long learning curve and extensive training requirements, the institution strives to keep IRB member turnover at a minimum.

Duties

Committee members are responsible for assuring that the rights and welfare of research subjects are protected, that risks are minimized and that benefits outweigh risks. Members vote to approve, require modifications (in order to secure approval) or disapprove submissions. These actions include: (a) initial reviews, (b) continuing reviews, (c) amendments, (d) serious adverse events, (e) sponsor serious adverse events (f) unanticipated protocol deviations, (g) advertisements, (h) consent form revisions (i) investigator brochure updates (j) protocol deviations, (k) minutes of previous meetings (l) investigator changes, (m) general policy issues and (n) non-compliance. The Committee has the authority to suspend or terminate an investigator's research privileges if it is determined he/she is non-compliant.

Attendance Requirements and Training

Members are required to attend meetings. All seven members have alternates. An alternate member may only substitute for his/her designated member. The IRB ensures that initial and continuing education requirements for the IRB Chair, IRB members, and IRB alternate members are met.

Annual Performance Evaluation

The IRB Chairperson considers the following criteria when evaluating IRB members: (a) thoroughness in reading of IRB meeting material; (b) level of participation in discussion; (c) meeting attendance; (d) does member provide appropriate representation for his/her professional background; (e) knowledge of human research protection regulations and guidelines; (f) dedication and sincerity to patient advocacy role.

Removal

The Chairperson is responsible for suspending or terminating membership of any individuals who are not fulfilling their member responsibilities or obligations.

VI. MANAGEMENT OF THE IRB

A. Meetings of IRB

The IRB meets fortnightly (with exceptions for holidays, weather, etc.) and meetings last approximately three hours.

B. IRB Administrative Support Staff

The organization employs one full time IRB Administrator/Secretary devoted exclusively to support IRB activities.

1. IRB Administrator/Secretary Duties:

(a) Directing and overseeing all IRB support functions and operations
(b) Training, supervising and evaluating IRB Staff
(c) Developing and implementing procedures to effect efficient document flow maintenance of all IRB records
(d) Maintain the official roster of IRB members
(e) Schedule IRB meetings
(f) Oversee the distribution of pre-meeting materials
(g) Prepare minutes of IRB meetings
(h) Prepare and distribute IRB Action Letters to investigators
(i) Maintain IRB documentation and records in accordance with regulatory requirements
(j) Assist new IRB members with orientation and training
(k) Facilitate communication between investigators and the IRB

(l) Serve as a resource for study staff on general regulatory information, and provide guidance about submission procedures
(m) Maintain training documentations and reference materials related to human subject protection requirements.
(n) Drafting reports to the IRB
(o) Assist in evaluation, audit, and monitoring of human subject research as directed by the IRB
(s) Keep manuals and SOP's up to date
(t) Assist with sponsor monitoring visits
(u) Coordinate and assist during regulatory inspections and site visits
(v) Copying study materials for distribution to IRB members

C. IRB Member Information on File

The IRB Administrator maintains information files for all IRB members. These files are stored in paper form in the IRB office and are electronically maintained as well.

(1) Name.
(2) Earned degrees.
(3) Representative capacity (*e.g.* physician, non-scientist, ethicist, community member).
(4) Indications of experience, such as board certifications, licensures, certifications, etc.
(5) Documentation of the voting status of each member.
(6) Documentation of alternate status.
(7) Committee member appointment letters

VII. IRB RECORD KEEPING & REQUIRED DOCUMENTATION

A. IRB Agenda and Minutes

The IRB agenda is prepared for each IRB meeting as submitted items are added to the agenda. Common agenda categories include the following:

- Conflict of Interest Disclosure Reminder - Members
- Minutes
- Quality Improvement
- Compliance
- Education
- Review of Non-Scripted Changes
- Initial Review
- Previously Tabled Protocol (Initial)
- Continuing Review
- Study Closure
- Dissemination of Study Results
- Consent Form Revision

Should researchers or their study staff need to review IRB files, the IRB staff will pull what is requested and provide a copy to the requestor. In the unlikely situation that an investigator and/or their research staff request permission to review their IRB record folders this may be done ONLY in the full-time presence of an IRB staff person.

All other access to IRB records is limited to those who have legitimate need for them as determined by the Director or Chairperson.

E. Long Term Record Retention

The IRB and investigators will keep a complete set of all research study records. The IRB and investigators will keep study records in accordance with hospital policy and as required by the protocol and regulatory law.

Research records are stored in secure research locations within the research center. *A "Certificate of Destruction" will be issued by the record storage facility and filed in the IRB office.* All Research records must be made accessible for review and copying by authorized officials of oversight regulatory body (DRAP).

F. Education and Training Records

Education and training records are kept in the IRB and Research Centre Office.

G. Communications to and from the IRB

Formal communications from the IRB are written and all determinations are conveyed in writing. Copies are filed in the IRB's investigator project file and are maintained in an electronic form too.

VIII. FUNCTIONS and OPERATIONS OF THE IRB

A. What Requires Review by the IRB?

If there is any element of research in any activity involving human subjects, the activity (including screening procedures and subject recruitment) must undergo IRB review before it can start. No study can be initiated until approved by the convened IRB or expedited reviewer (when appropriate).

B. Scheduling of Meetings

The IRB meets every two weeks in the IRB Conference room. Scheduled meetings will be canceled or re-scheduled for federal holidays, lack of a quorum or for cause at the direction of the Chairperson

C. Pre-meeting Distribution to Members of Agenda and Study Materials to be Reviewed

The IRB requires that all members receive all submission materials including minutes of the previous meeting in time to conduct a thorough review at convened meetings of all agenda items in order to determine if the research meets regulatory criteria for approval and for review of modifications to previously approved research in order to determine whether modified research (i.e. amendments) continue to fulfill the regulatory criteria for approval. One copy of the protocol, investigational brochure, approved consent form and any newly proposed consent form, amendment, advertisement, serious adverse event, continuing review, completed investigator submission forms or other material to be reviewed must be received in the IRB Office by a week before in order to be reviewed the following week. IRB staff prepare a written agenda, make copies of materials submitted by the investigator, and make copies of the previous week's IRB minutes for distribution to IRB members The schedule may be adjusted for holidays, weather or other unanticipated circumstance. Members are given a minimum of **four days to review materials.**

D. Review Process – Emsure Members Receive Review Material

1. All Members Receive Complete Study Documentation for Review
   Members receive personal copies of all study materials to be reviewed.
2. Ad Hoc Reviewers receive complete Study Documentation for Review
   Ad hoc reviewers receive personal copies of all study materials necessary to conduct a thorough review.

E. Monetary Management

The financial management of the committee shall be subservient to the policies of the Avicenna Medical College. There is an IRB processing fees of 500 USD per year or 800 USD for the duration of trial this fees is paid to Avicenna hospital only after the approval of the trail. IRB members maybe paid for the services rendered or an honorarium. Expenses, such as travel costs, may also be reimbursed.
IRB Members must keep in mind the liability of a future law suit and its responsibility towards the institute or the research worker. The fundamental purpose of IRB review of informed consent is to assure that the rights and welfare of subjects are protected. A signed informed consent document is evidence that the document has been provided to a prospective subject (and presumably, explained) and that the subject has agreed to participate in the research. ERC/IRB review of informed consent documents also ensures that the institution has complied with applicable regulations.

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Institutional policy, not any other regulation, determines whether compensation and medical treatment(s) will be offered and the conditions that might be placed on subject eligibility for compensation or treatment(s). Any statement that compensation is not offered must avoid waiving or appearing to waive any of the subject's rights or releasing or appearing to release the investigator, sponsor, or institution from liability for negligence.

There are regulatory requirements for submission of information which normally is included in the Investigator's Brochure. It is common that the Investigator's Brochure is submitted to the IRB, and the IRB may establish written procedures which require its submission. Investigator's Brochures may be part of the investigational plan that the IRB reviews when reviewing medical device studies.
It is not expected for the IRBs to routinely observe consent interviews, observe the conduct of the study or review study records. However, the IRB has the authority to observe, or have a third party observe, the consent process and the research. When and if the IRB is concerned about the conduct of the study or the process for obtaining consent, the IRB may consider whether, as part of providing adequate oversight of the study, an active audit is warranted.
When an IRB disapproves a study, it must provide a written statement of the reasons for its decision to the investigator and the institution. If the study is submitted to a second IRB, a copy of this written statement should be included with the study documentation so that it can make an informed decision about the study.
It is important that a formal line of communication be established between the Principal Investigator and the IRB. Principal Investigator should report adverse events directly to the responsible IRB, and should send progress reports directly to that IRB.

IX. IRB REVIEW/OPERATIONS

The IRB reviews all submitted items at a convened meeting. Reviews and determinations are documented in Committee minutes. Written notifications of review, approval, disapproval or actions required are sent to the investigator. Reviewed items along with a file copy of the written notification are filed in the protocol folder and kept in the IRB office.

A. Process

The IRB reviews and has the authority to approve, require modifications in (to secure approval) or disapprove all human research activities conducted at Avicenna Hospital. In order to secure IRB approval, the IRB must receive adequate information from the investigator and sponsor to determine:

1. that the research staff has appropriate qualifications and resources to conduct and monitor the study
2. that the protocol has scientific merit
3. that risks are minimized
4. that the risk-benefit ratio is appropriate (i.e. no research can be approved if potential risks outweigh potential benefits)
5. that selection of subjects is equitable
6. that provisions for safety monitoring are appropriate (should include plans for identification and reporting of adverse events and include safety assessment plans as applicable)
7. that provisions for privacy and maintaining confidentiality of data are appropriate
8. that vulnerable populations are afforded additional safeguards.

B. Continuing Reviews

The IRB is required to conduct continuing review of human subjects research at intervals appropriate to the degree of risk, but not less than once per year, except in the following cases:

Continuing review approval of research must occur **on or before** the date when approval expires. When continuing review is not completed prior to the expiration of the current approval period, there is an automatic lapse of IRB approval. All research must stop unless the IRB Chair determines that it is in the best interest of individual participants to continue the research interventions or interactions.

For research requiring continuing review, continuing Review is allowed to stop only when (1) the research is permanently closed to the enrollment of new participants, (2) All participants have completed all research-related interventions,

IRB chairperson can continue and approve the continuing review without the formal IRB meeting.

C. Lapse in Approval (STUDY EXPIRATION).

If a PI has not provided continuing review application materials to the IRB, or the IRB has not approved the continuing review application by the IRB approval expiration date, the IRB approval automatically lapses and all research activities must stop. No enrollment of participants can occur.

If the continuing review application is not approved by the IRB approval expiration date, all research activities must stop.

The IRB will notify the PI, the sponsor funding the project, affected participating sites, of lapses of study approval. Correspondence will be prepared by the IRB administrative staff to be reviewed and signed by the IRB Chair. Correspondence will be sent by encrypted email with a read receipt requested.

If the lapse occurred due to non-submission of the continuing review applications by the PI, the PI may submit the request for continuing review application, along with a justification for the delay in submission, up to 30 days after the expiration of approval date in order for the review to still be conducted by the IRB. After the 30 days have elapsed, the project or site will be considered noncompliant and the Board will proceed in accordance with reporting per the requirements outlined for reporting Serious and Continuing Noncompliance in this policy and consider the study or site for termination. If study or site termination is not in the best interest of participants, the study may be continued until the participants have safely completed the study or can be withdrawn but no new enrollment can take place.

If the PI wants to re-open a study that lapsed and it has been over 30 days since the lapse occurred, a new PI study application must be submitted, or the PI can consult with the IRB Administrative office regarding any documentation that may be required, in addition to the continuing review application, for the review to take place.

If the PI submitted all the required documents by the expiration date, but the approval period lapses, all the actions outlined above must still take place. The IRB will review the submitted materials as soon as practicable.

D. SAE Events

(Requirement - all IRB members receive personal copies of all study materials to be reviewed at convened IRB meetings)

Items submitted for review include but are not limited to:

- On-site SAE#
- Off-site Sponsor SAE#
- Date of event
- Description of event
- SAE relationship to study (related or not related)
- Is the event/risk anticipated or unanticipated
- Risk section of currently approved ICF
- Incorporation of new risks into a revised ICF (if indicated)
- Subject notification plans if indicated

E. Modification to Approved Research (Amendments)

It is the policy of the IRB that amendments or modifications in research projects may not be initiated without prior review and approval by the IRB, except where necessary to eliminate apparent immediate hazard to human participants

The Principal Investigator is required to submit the Modification to Approved Research to IRB including a justification for the amendment (signed), a complete description of the proposed changes, a summary of changes, and amended protocol as appropriate. Items submitted for review include but are but are not limited to:

- Protocol change (e.g. inclusion/exclusion, administrative, new information for subjects, therapy changes, scientific changes)
- Consent Form Change
- Advertisement
- Investigational Brochure and Safety Update Summary
- DSMB/Interim Safety Reports and Update Summary
- Investigator Change
- Reports of Unanticipated Problems involving risks to subjects or others
- Protocol Deviations
- Other

If the proposed amendment or modification involves the informed consent or conveying new information, the PI must indicate whether participants who have already consented to participate need to be re-consented and/or informed.

X. VOTING REQUIREMENTS

A. Quorum Required to Transact Business

Five IRB voting members must be present to achieve a quorum. Quorums can be lost if a member or members have to leave a meeting early or absent themselves due to conflicts of interest. In such circumstances affected projects would be deferred until a quorum was re-established or postponed until the next meeting. The IRB Administrator/Secretary is responsible for monitoring and ensuring the required quorum is maintained during IRB meetings, including special IRB membership requirements if research involves pregnant women, minors/children.

B. Full Voting Rights of all Reviewing Members

Each voting member has one vote.

C. Prohibition Against Conflict-Of-Interest Voting

Voting members who have conflicts of interests are required to recuse themselves from deliberations leave the room, and not vote. Conflicts of interest include circumstances where financial, professional, or other personal issues are involved.

XI. IRB CONDITIONS OF APPROVAL

(Note: A printed copy of IRB Conditions of Approval is mailed to investigators with each Initial and Continuing Review Approval Letter)

1. Do not initiate any research until you obtain written IRB approval that research can be initiated/continued. Adhere to ethical principles (1) Respect for persons, voluntary consent, privacy, confidentiality, (2) Beneficence - maximize possible benefits to the subject and minimize possible harms, (3) Justice - equitable selection of subjects.

2. The investigator will conduct the study according to the protocol, sound study design and (GCP) guidelines, applicable laws and regulations and will report to the IRB and sponsor significant findings that could affect the safety and well- being of research subjects. The investigator will prepare and maintain all study records including accurate case histories (e.g. case report forms and signed, dated consent forms along with Master Lists of research subjects for whom informed consent has been obtained as required by

the IRB).

3. Do not initiate any unapproved changes (*e.g.* Amendments, Consent Form modifications, Advertisements) without IRB review .Changes in Principal Investigator (PI), Sub Investigator (SI) and other study staff named in the protocol (e.g. medical monitor) require prospective IRB review and approval.

4. Informed, written consent is required of each human subject or his legally authorized representative (LAR). The investigator or a designee who has knowledge about the study, appropriate training and scope of practice obtains informed consent using an IRB approved and dated stamped consent form. The research subject or (LAR) and witness must sign and date the consent form.

Provide a copy to the subject or LAR signing the form and keep the original for your files.

XII. WHAT TO REPORT TO THE IRB, INSTITUTIONAL OFFICIALS AND OTHER REGULATORY AGENCIES

A. Unanticipated Problems Involving Risks to Participants or Others

This policy applies to all human subjects research conducted at Avicenna hospital, as well as investigators, IRB members and staff, and institutional officials. Others who may report possible unanticipated problems include participants, participant's family members, sponsors and other auditors.

Members of the research centre/project are required to report and the IRB is required to review reports of unanticipated problems involving risks to subjects or others (e.g. adverse events, complaints from participants or others, protocol deviations, new safety information, DSMB/data monitoring committee reports as well as any other event that influences the risk benefit analysis of the research. The IRB determines whether these reports were unanticipated problems involving risks to participants or others and takes required actions including notifications of subjects, suspension, termination and reporting to relevant institutional officials/entities (e.g. DRAP)

Definitions

Adverse Event (AE) - is any untoward physical or psychological occurrence in a human subject participating in research.

Related AE, Death or Problem – is an AE, death or problem that may reasonably be regarded as caused by or probably caused by the research.

Serious Adverse Event (SAE) - is an untoward occurrence in human research that results in death, a life-threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital anomaly, or birth defect., or that requires medical, surgical, behavioral, social, or other intervention to prevent such an outcome.

Unanticipated and Unexpected Problems – The terms refer to an event or problem in research that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population.

Examples of materials provided to and reviewed by IRB: - Unanticipated Problems. As warranted, the IRB may review relevant reports such as, protocol, investigational brochure, consent documents, IRB Continuing Reviews and protocol material deemed relevant. The IRB assesses reports of potential sources of unanticipated problems such as:

- complaints or violent or illegal behavior,
- loss of research data,
- breach of privacy or confidentiality,
- reports of injury or death involving participant or others including work related injury to personnel involved in human research
- a research participant becomes unexpectedly pregnant
- a research participant is incarcerated,
- interruptions of participant enrollments due to concerns about safety, rights and welfare of participants, research staff, or others,
- pharmacy or lab errors,
- scientific reports,
- interim data analyses including sponsor analyses describing a safety problem,

- DSMB, data monitoring committee findings describing a safety problem for which IRB/investigator action might be warranted,
- inability to conduct specified safety assessments,
- findings of scientific or ethical misconduct,
- sponsor monitor reports,
- protocol deviations, exceptions or violations, including changes to research without prior IRB approval in order to eliminate apparent immediate harm,
- compliance reports,
- internal and external adverse events that are unexpected involve new/increased risks, and related to research,
- any problem or deficiency involving substantive harm, or genuine risk of substantive harm, to the safety, rights, or welfare of human research participants, research staff, or others,
- any other information that influences the risk benefit analysis

IRB Review of SAEs and Serious Problems
Within 5 business days after receiving written notification of an SAE or serious problem, the IRB Chair or a qualified IRB member-reviewer must determine and document whether any actions are warranted to eliminate apparent immediate hazards to subjects.

(1) The IRB must review the incident and the determination of the IRB Chair or qualified IRB member reviewer at its next convened meeting and must determine and document that:

A. the incident was serious, unanticipated and related to the research,
B. there is insufficient information to determine whether the incident was serious and unanticipated and related to the research
C. the incident was not serious, and/or the incident was not related to the research

(2) Regardless of the determination, the convened IRB must also determine and document whether any protocol or consent form modifications are warranted. If modifications are warranted, the convened IRB must also determine and document whether or not previously enrolled subjects must be notified of the modification and, if so, when such notification must take place and how such notification must be documented.

Examples of actions the IRB may take as appropriate:

- Monitoring of research
- Modification of the protocol
- Modification of the information disclosed during the consent process
- Providing additional information to current participants (This must be done whenever the information may relate to the participant's willingness to continue participation)
- Providing additional information to past participants
- Requiring current participants to re-consent to participation
- Alteration of the frequency of continuing review
- Addition of continuing review
- Observation of the research or the consent process
- Requiring additional training of the investigator and study staff
- Notification of investigators at other sites
- Suspension or termination of the research according to IRB SOP "Suspension or Termination of IRB Approval" policy
- Obtaining additional information

B. Suspension or Termination of IRB Approval

- **Termination** – refers to a permanent halt in all research activities due to concerns about the safety, rights, or welfare of human subjects, research personnel or others regardless of whether the action to terminate was taken by an investigator, facility official, research review committee or external entity. Termination does not refer to interruptions for other reasons, including the expiration of project approval periods.

- **Suspension**- refers to a temporary interruption in selected research activity (e.g., new enrollments or specific interventions) due to concerns about the safety, rights, or welfare of human subjects, research personnel, or others regardless of whether the action to suspend was taken by an investigator, facility official, research review committee or external entity. Suspension does not refer to interruptions for other reasons, including the expiration of project approval periods.

- The IRB promptly notifies the principal investigator of the suspension.

- Once notified of the suspension, the principal investigator must immediately submit to the IRB Chairperson, a list of research participants for whom suspension of the research would cause harm. The IRB Chairperson, with appropriate consultation with the determines if the participants may continue in the research.

- If study approval is terminated the IRB must determine if enrolled participants should be notified. The IRB considers their rights and welfare when determining procedures for withdrawal. When follow-up of participants for safety reasons is deemed necessary, participants are informed and

any subsequent adverse events that may occur will be reported to the IRB and sponsor.

- Once suspended or terminated the IRB review and re-approval must occur prior to re-initiation of the research.

- Suspensions and terminations do not include interruptions in research resulting solely from the expiration of a protocol approval period

C. Research Misconduct

Definition

- Fabrication is making up data or results and recording or reporting them.
- Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.
- Research misconduct does not include honest error or differences of opinion.
- The standard response to a research misconduct allegation involves a threshold determination, an initial Inquiry, and a formal Investigation conducted by the facility where the research in question is located. Based on the Investigation's findings and conclusions, the Facility Director adjudicates (determines the outcome of) each case of research misconduct. Respondents found guilty of research misconduct have an opportunity to appeal the findings and recommended corrective actions.

XIII. THE INFORMED CONSENT PROCESS

(In order to approve research, the IRB ensures that the consent process meets the criteria for approval)

1. No human being can participate as a research subject unless legally effective informed consent of the subject or the subject's LAR has been obtained. Documented informed consent is required from research participants prior to initiating any research activities including recruitment and screening procedures. The informed consent process begins prior to the conduct of any research procedures (including screening procedures) and must be conducted in a language that subjects and legally authorized representatives (LAR) can understand. The investigator or an approved study staff designee who has knowledge about the study, appropriate training and scope of practice must obtain informed consent using the IRB currently approved and date stamped consent form. The research subject or (LAR)and witness, if required by the IRB, must carefully review the consent document, and sign and date the most current IRB approved consent form version. Authorized study staff who are obtaining consent are available to answer questions throughout the consent process. Subjects and LARs must not be coerced and must be given ample opportunity to consider whether to participate – **no subject or LAR should be forced, coerced, or unduly influenced to participate.** Subjects and LARs must be kept informed

throughout the research study and after, as appropriate, of significant new information that might impact subject safety. Legally Authorized Representative is, "an individual or judicial or other body, authorized under applicable law to consent on behalf of a prospective subject to the subjects participation in the procedure(s) involved in the research Copies of ICF are given to subject or LAR.

2. The IRB ensures that the informed consent form includes required elements and that it is consistent with the protocol. The IRB considers risks and benefits that may result from the research and distinguishes risks of research activities (including screening tests) from the risk of therapeutic activities (i.e. usual care). Identification of probable individual and societal benefits are assessed.

3. The IRB has the authority to observe and monitor the consent process and the research. Investigators are required to allow internal and external auditors to review their study files and to observe study procedures as appropriate to verify compliance with DRAP regulations and ICH GCP guidelines.

4. The process for obtaining informed consent is systematically evaluated during Initial Review and includes review of the investigator plan for: (a) Assessing capacity to consent, (b) Ensuring information is given to the subject or their designated LAR in a language that is understandable to the subject or representative, (c) Providing the prospective subject or the designated LAR sufficient opportunity to consider whether or not to participate and be given an opportunity to ask questions or voice complaints - contact numbers for study staff must be included in the consent form, and (d) Ensuring that subjects give consent without coercion or undue influence and that study participation is voluntary.

XIV. COMMUNICATION FROM THE IRB

IRB determinations will be communicated in writing to the investigator. Official IRB correspondence is maintained in computerized form and hard copy file.

A. To the Investigator for Additional Information

The IRB may request additional information from the Principal Investigator or sponsor to enable appropriate review. Investigator responses should be received within 30-60 days unless an earlier response is required due to a subject safety issue.

B. To the Investigator Conveying IRB Decision

IRB determinations are conveyed to the Principal Investigator in writing within one week of the IRB meeting and include actions required if applicable.

C. To Sponsor of Research Conveying IRB Decision

The IRB normally does not notify sponsors of IRB determinations. The Principal Investigator serves as the communications link between the IRB and the sponsor. There may be circumstances where the IRB feels it is necessary to directly notify the sponsor (*e.g.* suspension, termination).

XV. APPEAL OF IRB DECISIONS AND COMPLAINT PROCESS

A. Criteria for Appeal

Investigators may appeal IRB decisions. Appeals should be accompanied by a cover letter that explains the basis of the appeal. Principal Investigators, study coordinators and/or sponsor representatives may attend, or be requested to attend an IRB meeting. Investigators and coordinators are encouraged to contact IRB staff and IRB members to discuss concerns without compromising the integrity of the process.

B. To Whom Appeal is Addressed

IRB Chairperson –Institutional Review Board., Avicenna Hospital

XVI. INVESTIGATOR RESPONSIBILITIES

A. Professional Qualifications and Responsibilities

Investigators are responsible for oversight and management of all aspects of the research as outlined in the IRB approved protocol and as conducted by the research staff. Investigators must effectively communicate with the IRB and respond to requests from the IRB in a timely manner. S/he must be available to the IRB during meetings and/or reviews.

The IRB requires the submission of curriculum vitae for all study staff and requires that mandatory training be completed. Additional research training may be required prior to conducting research activities. If the IRB determines that the Principal Investigator and/or key research staff do not have the professional qualifications or resources necessary to conduct research in accordance with regulations this can be the basis for disapproval or a stipulation to involve individuals with appropriate expertise in the study. The IRB may consider investigator collaborations with other professionals who have the required expertise and who agree to serve as sub-investigators, preceptors, mentors, or medical monitors.

B. Investigator Responsibilities - Maintenance of Research Records

It is the investigator's responsibility to maintain research records. This means maintaining written documentation on file that the protocol is being implemented as approved by the IRB and in accordance with other required approvals.

C. Study Protocol

The IRB addresses many complex, overlapping and intermingled issues dealing with the basic question, "is there any possible benefit from this study and does the potential gain outweigh the potential risk?" In order to judge if criteria are met the Committee needs detailed information. If a protocol is submitted for review and Committee members believe that there is insufficient information to enable an appropriate review, a written request for additional information will be

sent to the Principal Investigator. The investigator is responsible for the research protocol and for ensuring research compliance.

Initial and Continuing Review require investigators to provide detailed information about their proposed research

1. Complete protocol (including questionnaires, surveys and data collection tools).
2. Consent form and details about the process (e.g. capacity to consent).
3. Title of the study.
4. Purpose of the study.
5. Sponsor of the study including addresses.
6. Sponsor obligations regarding safety information notification.
7. FDA Form 1572 (drug), Investigator Agreement
8. Results of previous related research.
9. Study design, scientific rationale, and study purpose.
10. Description of subject inclusion/exclusion criteria, enrollment and recruitment plans.
11. Description of the informed consent process, to include informed consent forms
12. Investigator risk-benefit assessment and risk designation. Consider potential risks and potential benefits including physical, psychological, economic, social/legal and privacy risks.
13. Description of plans to minimize risk.
14. DSMB and/or other data safety monitoring
15. Plans to protect privacy and confidentiality of data.
16. Investigational Brochures and package inserts.
17. Randomization plans.
18. Provisions to identify, monitor and report serious adverse events.
19. Subject selection.
20. Payments to subjects for their participation and payment terms.
21. Medical treatment and compensation for injured research subjects.
22. How and where research data will be collected & stored.
23. Disclosure of conflicts of interest.
24. Adequacy of research resources to conduct the proposed project.
25. For study research staff description of the role in study and scope of duties.
26. Completion of training requirements.
27. Impact of research on other hospital services (financial and access).

D. Subject Recruitment

In order to approve research, the IRB must determine that selection of subjects is equitable. The IRB requires investigators to submit for review the final copy of all advertisements and recruitment incentives associated with the research that they oversee.

IRB recruitment procedures are designed to assure that informed consent is given freely and to avoid coercion or undue influence. To evaluate this the IRB needs to obtain appropriate information in order to know from what population the subjects will be drawn, what incentives are being offered, and the conditions under which the offer will be made.

E. Equitable Selection of Subjects

To approve research, the IRB must determine that the selection of subjects is equitable. In making this determination, the IRB should evaluate the purposes of the research, the research setting, and the inclusion/exclusion criteria.

(1) Purposes of research.
The purposes of the research are evaluated by the IRB during Initial Review. The IRB documents if the purpose is appropriate and if it should yield useful information.

(2) Setting in which research occurs.
Investigators are required to specify the study site in their Initial Review submission. The role of participating institutions, IRBs, and off-site research personnel including how they communicate with each other must be provided to the IRB for review. The IRB evaluates if adequate plans are in place to minimize potential risks due to lack of communication or misunderstanding of responsibilities between research sites. As part of its review the IRB evaluates the standard informed consent process to determine if modifications are required in order to minimize risks. The IRB may require as appropriate a formal inter-institutional agreement. Details of the IRB review and approval for off-site research are documented in IRB minutes and investigator correspondence.

F. Subject Selection Criteria

Includes consideration that risks, burdens and benefits of research are distributed fairly. Includes consideration of:

1. Purposes of research.
2. The burdens and risks of the research.
3. Potential benefits of the research.
4. Inclusion criteria.
5. Exclusion criteria.
6. Vulnerable populations.
7. Projected enrollment.
8. Methods to identify and recruit subjects.
9. Nature of the information sought.
10. Subject payment.

G. Subject Enrollment

Includes evaluation of the following:

1. Projected enrollment and number of subjects entered into the study.
2. Gender of subjects entered into the study.
3. Number of women entered into the study.
4. Minority status of subjects entered into the study.
5. Names of subjects entered into the study.
6. Enrollment of vulnerable subjects.

H. Investigational Brochure

The Investigational Brochure and/or package inserts will be provided to members prior to the convened meeting when the relevant protocol is to be reviewed.

I. Case Report Forms

The case report form that is provided by the sponsor will be reviewed by the IRB

J. Proposed Informed Consent Document – Documentation

Basic Elements of Informed Consent

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others that may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject;

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled; and

(9) One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

(i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or

(ii) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

When Participants Withdraw From a Clinical Trial IRB Determines:

- When a participant withdraws from a study, the data collected on participant to the point of withdrawal remains part of the study database and may not be removed. It is advised that the consent document should not give the participant the option of having data removed to maintain the integrity of the science.
- A researcher may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the participant distinguishes between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the participant's information.

- If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent. However, a researcher may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.