



# **Sponsor/Investigator IRB Requirements and Guidebook**

Version Date: September 2011

Confidential

## Purpose of the Guidebook

To provide knowledge and guidance to sponsors, investigators and their staff who will be involved in human research studies.

## Introduction

This guidebook will provide a basic understanding to sponsors, investigators and their staff of what their role and responsibility will be while conducting human research studies. Alpha IRB's goal is to provide the information needed to protect the rights and welfare of every single research subject.

## What Requires IRB Review

Regulations require IRB review and approval for *research involving human subjects* if it is funded or regulated by the federal government. Federal regulations define research as: "a systematic investigation designed to develop or contribute to generalizable knowledge." [45 CFR 46.102(d)]

### *Definition of a Human Subject*

Individuals whose physiologic or behavioral characteristics and responses are the object of study in a research project.

**Under the federal regulations**, human subjects are defined as: living individual(s) about whom an Investigator conducting research obtains:  
(1) data through intervention or interaction with the individual; or  
(2) identifiable private information [Federal Policy §46.102(f)].

If an investigator is unclear about whether a planned activity is research, the investigator should contact Alpha IRB at: 949-542-3882 for assistance.

## **Responsibilities of Sponsor and/or Principal Investigator and their Research Staff**

- Understand the ethical standards and regulatory requirements governing research activities with human subjects.
- It is the responsibility of the investigator to be cognizant of any local or State law(s) that may affect the conduct of human subject research in his/her state and apply these rules appropriately. The IRB may require that such knowledge and application be demonstrated before IRB approval is issued for studies involving certain populations and procedures.
- Inform research staff of the regulations governing research and the institutions research policies.
- Ensure that all research activities have IRB approval and other approvals required by the institution before human subjects are involved.
- Implement the research activity as it was approved by the IRB.
- Obtain the informed consent of subjects before the subject is involved in the research and document consent as approved by the IRB.
- Maintain written records of IRB reviews and decisions and obtain and keep documented evidence of informed consent of the subjects or their legally authorized representative.
- Obtain IRB approval for any proposed change to the research protocol prior to its implementation.
- Comply with the IRB requirements for timely reporting of unanticipated problems involving risks to participants or others including applicable serious adverse events, safety reports received from the Sponsor, or data safety and monitoring summary reports and significant protocol deviations.
- Obtain continuation approval from the IRB on the schedule prescribed by the IRB.
- Make provisions for the secured retention of complete research records and all research materials.
- Ensure the confidentiality and security of all information obtained from and about human subjects.

- Notify the IRB regarding the emergency use of an investigational drug or device within 5 working days of the administration of the test article.


## **Possible Actions if IRB Regulations are Not Followed**

- Suspension of research project.
- Suspension of all of a Principal Investigator's research projects.
- Inability to use data or publish results.
- Notification of sponsors, regulatory agencies and funding agencies of noncompliance.
- Debarment by FDA from using investigational products.
- Inability to receive funding from federal grants.
- Additional monitoring and oversight by the IRB and/or third party monitoring of research activities.
- Termination of employment.
- Loss of licenses.
- Immediate shut-down of ALL research at an organization.

## **Submitting a Research Study**

Alpha's Independent Review Board (IRB) meets twice a week on Monday and Wednesday for Full Board review. Submission materials must be received by 3:00pm Pacific Time (PT) on the preceding Tuesday for Mondays meeting and the preceding Thursday for Wednesdays meeting. Submissions may be sent as hard-copy or electronically preferably entered online using **OASIS** (Online Access Study Information System).

To access **OASIS** go to: <http://www.alphairb.com/>

Click on  the link at the bottom right hand corner of the screen to start submitting your study.

***Remember, your Study Management Specialist is always available to assist you in navigating the system or answering any questions.***

The review process will begin when Alpha IRB receives the complete submission. Incomplete submissions may not be placed on the agenda for the next meeting, so Sponsor/Investigators should review the IRB review process and the guidelines on the application forms for each type of submission. Submission forms are available on-line, via e-mail, or hard copy.

**Basic components of an IRB submission – All Alpha IRB Forms are available on our website at: [www.alphairb.com](http://www.alphairb.com)**

### **Submission Materials**

- Sponsor/CRO Study Application
- Research protocol – A detailed research protocol is required for IRB review of your research.
- Investigator Brochure or Package Insert/Device Manual/Description (Required for FDA regulated products)
  - Alpha IRB is required to examine these items in order to adequately assess the risk/benefit ratio for subjects participating in the research.
- Informed Consent Form, Genetic, HIPAA, Assent, etc.
- Proposed subject instructions
- Other supporting material (sample of proposed advertising, patient diaries, etc.)
  - Alpha IRB is required to review any advertisements, flyers, Internet postings, etc., for subject recruitment, correspondence to subjects or other cooperating individuals such as referring physicians or facilities.
  - In addition, Alpha IRB reviews all press releases intended to facilitate recruitment of subjects. Contact documents are not approved or valid without an IRB approval.

- If possible include recruitment materials with your initial application. If the material is not ready at the time of initial application, submit recruitment material when it is available and prior to use, but allow sufficient time for revisions prior to publication.
- Advertisements, press releases, etc., may qualify for expedited review.
- Surveys, Questionnaires, Etc.
  - Alpha IRB is required to review all research instruments such as surveys, questionnaires, etc. If the instrument is used regularly in standard practice, it is not necessary to submit the instrument.
- Recruitment Bonuses
  - Alpha IRB strongly recommends that the investigator carefully evaluate bonus payments offered by the sponsor for additional subject recruitment, beyond the original contractual agreement. Bonus payments or other incentives, such as medical equipment, may cause undue influence on the investigative staff, when the staff is recruiting study subjects. The IRB should be consulted on all bonus payments outside of the initial contract.

## **Informed Consent**

The outline for informed consent can be found in The Code of Federal Regulations 45 CFR 46.116(a) and 21 CFR Part 50.25(a).

### **Obtaining Informed Consent**

- Provide subject with the approved informed consent to read through in a quiet location.
- Discuss study procedures thoroughly with subject.
- Ensure the subject understands by answering questions the subject may have.
- Encourage subject to discuss concerns with doctor, staff, family and friends.
- Obtain the voluntary agreement of the subject to participate in the study.

- Give the subject a copy of the signed informed consent and bill of rights (if applicable in your state) and encourage them to call if any further questions arise.

### **Ensuring Understanding**

- Provide consent in a language that is understandable to the subject or his/her representative.
- Provide non-English speaking subjects a translated informed consent document that is accurate as determined by the IRB.
- If a translator is used, providing a written translation of the consent document is still required.
- Give the person enough time to think about the research before consenting to research study participation.

### **Obtaining Voluntary Agreement to Participate**

- Shall be obtained from the subject or the subject's legally authorized representative.
- Shall be obtained under circumstances that provide the subject with an opportunity to consider whether or not to participate and that minimize coercive influences.
- Coercive tactics such as inappropriate financial or other rewards cannot be used. Illiterate English-speaking subjects can "make their mark" on the informed consent document, as long as it is consistent with applicable state laws.

### **Waiving Informed Consent**

In certain circumstances, the IRB may waive the requirement to obtain informed consent if the Board finds that the research meets specific criteria that is in accordance with provision at 45 CFR 46.116(c) and (d), 21 CFR 50.23 and 24.

## Medical Device

### SIGNIFICANT RISK AND NON-SIGNIFICANT RISK DEVICE STUDIES

#### A. What is a Significant Risk Device Study?

Under 21 CFR 812.3(m), an SR device means an investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

#### B. What is a Non-significant Risk Device Study?

- An NSR device study is one that does not meet the definition for an SR device study.

## Device Study Submission

Provide the following:

- Device manual/description and **ONE** of the following:
  - **FDA Letter** granting the Investigational Device Exemption (IDE).

- **Statement from sponsor** stating that the study is a non-significant risk device study. \*A template letter is provided below.

Or

- **Letter explaining why the investigation is exempt.**

## NON-SIGNIFICANT RISK STATEMENT (Template)

Date:

Protocol No:

Sponsor/Investigator:

Address:

The investigational device \_\_\_\_\_ we feel does not have significant risk based on the criteria listed below:

- It is **not** intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;

**Please provide an explanation of why this device meets this criterion:**

- Is **not** purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;

**Please provide an explanation of why this device meets this criterion:**

- Is **not** for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or otherwise presents a potential for serious risk to the health, safety, or welfare of a subject

**Please provide an explanation of why this device meets this criterion:**


Printed Name: \_\_\_\_\_ Date: \_\_\_\_\_

Signature: \_\_\_\_\_

## Submitting an Investigator's Site

Alpha's Independent Review Board (IRB) meets twice a week on Monday and Wednesday for Full Board review. Submission materials must be received by 300pm Pacific Time (PT) on the preceding Tuesday for Mondays meeting and the preceding Thursday for Wednesdays meeting. Submissions may be sent as hard-copy or electronically preferably entered online using OASIS (Online Access Study Information System).

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Click on  the link at the bottom right hand corner of the screen to start submitting your study.

***Remember, your Study Management Specialist is always available to assist you in navigating the system or answering any questions.***

The review process will begin when Alpha IRB receives the complete submission. Incomplete submissions may not be placed on the agenda for the next meeting, so Sponsor/Investigators should review the IRB review process and the guidelines on the application forms for each type of submission. Submission forms are available on-line, via e-mail, or hard copy.

**Basic components of an IRB submission – All Alpha IRB Forms are available on our website at: [www.alphairb.com](http://www.alphairb.com)**

The following are a list of requirements for site submission.

- Site Submission Form
- Medical license
- Investigator's Current Credentials (CV)
- SOP's (Consenting Process)

- Delegation Form (if other than the investigator/sub-investigator will be consenting subjects) (attached)
- 1572 (if drug study)
- Additional Consenting Measures if enrolling vulnerable population (if applicable)
- FDA Audit Information (if applicable)
- Financial Disclosure (if applicable)

## **HIPAA – Health Insurance Portability and Accountability Act**

Protected Health Information (PHI) is defined under HIPAA as individually identifiable health information. Identifiable refers to data explicitly linked to a particular individual as well with data that could enable individual identification.

**Identifiers include but are not limited to:** name, Social Security number, street address, birth date, telephone number, email, medical record number, health plan number, driver's license number, full face photography, etc.

### **Valid Authorizing Elements**

- A description of the PHI being used.
- A statement of the purpose of the use of PHI.
- A list of those who can use the PHI.
- A list of those who can receive the PHI, including the possibility of re-disclosure.
- A statement that once PHI is disclosed by the recipient it may no longer be protected by the Privacy Rule.
- Information about the expiration of the authorization.
- Information about the right to revoke the authorization.

### **Authorization Under the Privacy Rule Regulations**

Alpha IRB, as a central IRB, does not have authority to approve or disapprove authorization language under HIPAA regulations. This is a regulatory

responsibility of any research site that are Covered Entities under 45 CFR 160 and 164. If Authorization is included in the consent document, Alpha IRB will review it for compliance with regulation as 21 CFR 50 and 56 and /or at 45 CFR 46. The sponsor should address their requirements regarding accessibility of data in their contract with each Covered Entity.

## **Conflicts of Interest**

Alpha IRB is concerned about the potential for abuse when Investigators have a financial obligation or interest that may pose a conflict of interest. Alpha IRB requires that Investigators disclose within their application all potential financial conflicts of interest and explain how the potential conflict of interest will be minimized or resolved. In these situations, Alpha IRB may require disclosure of conflicts of interest in consent forms.

## **Ethical Conduct**

Alpha IRB expects that all research will be conducted in accordance with the principles of the Belmont Report.

### **MONITORING OF INVESTIGATIVE SITES**

As sponsors routinely monitor investigative sites, they are in a unique position to uncover information to which the IRB may not otherwise be privy. Alpha IRB requests that the sponsor provide Alpha IRB with any information that may affect the rights and welfare of participants, or their willingness to continue participation. Such information may be contained within a monitoring report, or may be summary of the sponsor's assessment. Alpha IRB will then work with the sponsor to rectify the situation. In addition, Alpha IRB may conduct its own monitoring visit to investigative sites. Alpha IRB selects sites to visit, based on certain criteria, such as the conduction of a high risk study, or the enrollment of a vulnerable population. Alpha IRB may also conduct a for-cause visit, or may randomly select a site to visit. Results of concern will be shared with the sponsor.

## The Review Process

Under federal regulations, there are three possible IRB review procedures:

- **Full Committee Review** – *Most studies are reviewed by the full IRB.*
- **Expedited Review**
- **Review for Exemption Status**

### Full Committee Review

Full committee review is the standard type of review described in the Federal regulations. It must be used for the initial review of all studies that are not eligible for expedited review or exemption status. Alpha IRB employ's a "primary reviewer system" which all IRB members receive basic information about the research application, but a "primary reviewer" with experience and/or expertise in the study area is assigned to conduct a thorough review of the IRB application and any accompanying documentation. The "primary reviewer" will then report his/her findings for discussion at a convened meeting of the full board.

### **Procedures and conditions for full committee review require that:**

- The review must be conducted at a convened meeting of the IRB. A majority of IRB members (a quorum) must be present at the meeting
- At least one member whose primary concerns are in nonscientific areas must be present at the meeting (in addition, FDA policy requires that a physician be present).
- In order to approve research, the IRB must determine that all of the requirements specified in 45 CFR 46.111 (and if applicable, 21 CFR 56.111) are satisfied.
- A majority of the members present at the meeting must approve the research.

- IRB members who have a **conflict of interest** in a research project may provide information to the IRB, but cannot participate in the review. Members with a conflict do not count toward the quorum for that review.
- The IRB must notify investigators in writing of its decision to approve, modify or disapprove the research.
- IRBs must keep detailed documentation of meeting activities including attendance, voting on actions, the basis for the actions, and a written summary of the IRB discussion of controverted issues and their resolution.

### Expedited Review

Alpha IRB may determine that your study qualifies for expedited review if the study meets criteria for Expedited Review.

Under an expedited review procedure, the review may be carried out by the IRB Chairperson or by one or more experienced reviewers designated by the Chairperson from among members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non–expedited procedure set forth in [§46.108\(b\)](#).

Federal Regulations established the following 9 categories that IRBs may use to invoke the expedited review process. The research may not involve more than "minimal risk".

- (1) Clinical studies on drugs or medical devices for which an investigational new drug (IND) or an investigational device exemption (IDE) application is NOT required. Similarly, a study with a cleared/approved medical device that is being used in accordance with its cleared/approved labeling.
- (2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture.
- (3) Prospective collection of biological specimens for research purposes by noninvasive means.

- (4) Collection of data through noninvasive procedures routinely employed in clinical practice provided that:
  - The noninvasive procedure must not involve general anesthesia or sedation routinely employed in clinical practice or procedures involving x-rays or microwaves.
  - Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.
- (5) Research involving data, documents, records, or specimens that:
  - Have been collected.
  - or
  - Will be collected solely for non-research purposes (such as for medical treatment or diagnosis).
- (6) Collection of data from voice, video, digital, or image recordings made for research purposes.
- (7) Research on individual or group characteristics or behavior.
- (8) Continuing review of research previously approved by the convened IRB where:
  - The research is permanently closed to the enrollment of new subjects; all subjects have completed all research-related interventions; **and**, the research remains active only for long-term follow-up of subjects,
  - **Or where:** No subjects have been enrolled and no additional risks have been identified.
  - **Or where:** The remaining research activities are limited to data analysis.
- (9) Continuing review of research not conducted under an investigational new drug (IND) application or investigational device exemption (IDE) and where categories two (2) through eight (8) do not apply.

## Claim of Exemption

Federal regulations specifically define 6 categories of human subject's research that are exempt from the other provisions of the regulations. Federal Guidance indicates that applying exempt status to a project is a decision to be made by the IRB and that investigators cannot make this determination for themselves.

Research activities in which the only involvement of human subjects is in one or more of the categories listed below:

- 1) Research conducted in established or commonly accepted educational settings, involving normal educational practices.
- 2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior.
- 3) Research not exempt under "2" above, may still qualify for an exemption if the human subjects are elected or appointed public officials or candidates for public office.
- 4) Research involving the collection or study of freely available de-identified existing data, documents, records, pathological specimens, or diagnostic specimens.
- 5) Research and demonstration projects conducted by heads of government departments or agencies which are designed to evaluate public programs.
- 6) Taste and food quality evaluation and consumer acceptance studies.

**NOTE:**

A Claim of Exemption does not necessarily exempt Investigators from the requirement of gaining written informed consent from subjects. Most research requires the use of an informed consent form. For studies where there are no subject identifiers, i.e., anonymous data is collected; an information sheet or

## **Notification of Board Actions**

Alpha IRB will communicate the results of the review directly to the responsible member of the clinical research team by e-mail, fax or phone within 24 hours of study review. Sponsor/Investigator is asked to respond to questions or requested revisions to a study or study material within 90 days of the review.

## **Determinations**

Alpha IRB will make one of the following determinations as a result of its review of research submitted for initial review or for continuing review:

1. **Approved:** The protocol and accompanying documents are approved as submitted. Final approval will commence on the day the study is approved by an action of the convened IRB or Chairperson or designee and expire within one (1) year of the meeting date, but not later than the day preceding the date of review.

Approvals are always considered conditional. The conditions for continued approval, and the time frame (if any) within which they must be met will be clearly stated in the approval letter. If the conditions of the approval are not met, approval may be withdrawn. Investigators must receive their approval letter from the IRB before they initiated any procedures that are related to the protocol. The IRB expects the sponsors to use investigators who understand and adhere to the federal requirements regarding IRB review and approval.

*It is the responsibility of the investigator to be cognizant of any local or State law(s) that may affect the conduct of human subject research in his/her State and apply these rules appropriately. The IRB may require that such knowledge and application be demonstrated before IRB approval is issued for studies involving certain populations and procedures.*

## **After Initial Approval**

When written approval is issued by Alpha IRB, investigator can initiate the study procedures. However, continued approval is always conditional. Standard conditions for continued approval are:

- Any changes in the research protocol, informed consent document, or subject information during the approval period must be submitted to the IRB for review and must not be initiated until approved by the IRB.
- All advertisements, letters and any other media for subject recruitment must be submitted and approved prior to use.
- Significant deviation from the research protocol and/or instances of non-compliance must be reported to the IRB as soon as possible, but no later than **ten (10) business days** from the date the site became aware of the event.
- All unanticipated problems that may involve risk to participants or others must be reported to the IRB as soon as possible, but no later than **ten (10) business days** from the date the site became aware of the event.
- A copy of the approved informed consent document must be signed and dated by each subject or the subject's legal representative prior to initiation as *any* study procedures. In addition, each subject must be given a copy of the signed consent form and subject's bill of rights (if applicable in your state).
- The investigator must cooperate with the IRB in its efforts to conduct continuing review.

The IRB may elect to place additional, specific conditions on the conduct of a study.

## 2. Conditionally Approved:

Minor modification of, or addition to, a protocol or accompanying documents is required. Changes will be voted upon during the IRB's meeting, as well as the terms of approval. The Investigator will be informed in writing of the required changes and requested information and must provide the IRB with the changes or information.

The Chairperson or his/her designee has the authority to review the information via expedited review unless the IRB requires that the material or

information be reviewed by the full IRB, the primary reviewer or another individual delegated by the IRB to review the response. Upon satisfactory review, approval will be issued as of the date that the requested information or materials are approved. However, the expiration date will be based on the date of the initial IRB review. Subjects must not be recruited into the study until final approval has been issued.

3. **Tabled**: Significant questions are raised by the proposal requiring its reconsideration after additional information is received from the Sponsor and/or Investigator.

4. **Disapproval**: The proposal fails to meet one or more of the criteria used by the IRB for approval of research. Disapproval cannot be given through the expedited review mechanism and may only be given by majority vote at a convened meeting of the IRB.

Investigators have the right to discuss IRB requests for revision and decisions of disapproval directly with the Committee. The IRB, however, retains the final authority for approval of proposed research with human subjects.

The IRB review process allows Investigators various levels of appeal from the time a study receives initial review through approval or disapproval. Any and all IRB decisions are contingent upon the response of the Investigator. If the IRB finds that the negotiation is at an impasse, they may request an intramural and/or extramural independent consultant review. The IRBs wish to respect the Investigator's intellectual property, therefore, prior to assigning a consultant; Investigators are asked if there is anyone they would NOT like to review their study.

## **Investigator Responsibilities Once a Study is Approved**

### **Record Keeping**

The signed informed consent document is one of the most critical research records the investigator needs to obtain and keep. It provides verification that the research was explained to the subject and that the subject understood and

voluntarily agreed to participate in the research study. Investigators are responsible for retaining signed consent documents, IRB correspondences, and research records for at least 3 years after the completion of the research activity.

### **Unanticipated Problems**

Alpha IRB requires the reporting of any events determined by the Investigator and/or Sponsor to be unanticipated problems involving risk to participants or others. Alpha defines this as any problem, event, or new information that meets all of the following criteria:

- 1) The event is **unexpected** (in terms of nature, severity, or frequency) given:
  - a) the research procedures that are described in the protocol–related documents, such as the IRB–approved research protocol and informed consent documents; and
  - b) the characteristics of the subject population being studied,
- 2) The event is **related or possibly related** to participation in the research (*possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research)
- 3) The event suggests that the research places participants or others at a **greater risk of harm** (including physical, psychological, economic, or social harm) than was previously known or recognized.

Events that meet all of the above criteria need to be reported to Alpha IRB promptly, but no later than **ten (10) business days** from the date the site became aware of the event by completing the “Serious Adverse Event / Unanticipated Problems Report Form” available on the Alpha IRB website at: [www.alphairb.com](http://www.alphairb.com).

If the event (adverse or otherwise) does not meet all 3 of the above criteria, the event is not required to be reported to Alpha IRB. The Investigator must use

his/her clinical judgment in determining whether an event occurring at their site is a problem that meets all the above criteria.

For multicenter trials, Alpha IRB recognizes that the sponsor is in a better position to process and analyze adverse event information for the entire study and to assess whether an adverse event occurrence is an unanticipated problem involving risk to participants or others. Therefore, for the submission of multicenter trial reports such as IND Safety Reports, Medwatch Reports, CIOMS Reports, etc., Alpha IRB requires that the submission clearly indicate whether the event is considered to represent an unanticipated problem involving risk to participants or others and if so, what actions are being implemented in response. Multicenter reports where it is determined that the event does not represent an unanticipated problem involving risk to participants or others are not required to be submitted to Alpha IRB.

For further information regarding the reporting guidelines for adverse events and unanticipated problems, please review the FDA Guidance Document entitled, ["Adverse Event Reporting to IRBs — Improving Human Subject Protection," dated January 2009.](#)

Possible examples of an unanticipated problem include, but are not limited to:

1. Serious adverse event that is both unexpected and related to the research
2. Serious Problem (local only) that results in:
  - Substantive harm or damage (or risk of substantive harm or damage) to the safety, rights, or welfare of research subjects, research staff, or others: or
3. Information that indicates a change to the risks or potential benefits of the research for example:
  - An interim analysis indicates that the participants have a lower rate of response to treatment than initially expected.
  - Safety monitoring indicates that a particular side effect is more severe or more frequent than initially expected.

- A paper is published from another study that shows that an arm of the research study is of no therapeutic value.
- 4. A breach of confidentiality.
- 5. Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
- 6. Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant.
- 7. Incarceration of a participant in a protocol not approved to enroll prisoners.
- 8. Event that requires prompt reporting to the sponsor.
- 9. Complaint from a participant when the complaint indicates unexpected risk or cannot be resolved by the research team.
- 10. Protocol violation (which an accidental or unintentional change to the IRB– approved protocol) caused harm to participants or others or indicates that the participants or others are at an increased risk of harm.
- 11. Sponsor–imposed suspension for risk.

### Amendments

- All amendments, including changes to consent forms, changes in study personnel, and deviations in the protocol must be reported to Alpha IRB
- All modifications to currently approved research are required to have IRB review and approval prior to implementation.
- An amendment may require full IRB review if the modification is significant and affects the risks and benefits to subjects in the research. Changes in the risks or benefits to subjects may require modifications to the consent form and re–consenting of subjects.
- Minor changes that do not increase the risk to research subjects may receive an expedited review. If appropriate, the Chairperson or designee will review the changes to determine if they qualify for expedited review.
- Amendments include but are not limited to consent forms, protocols, Investigator Brochures, study instruments, recruitment tools, study personal,

deviations, etc.

- The IRB may only approve modification submitted during a current approval year to the end of that period. For example, if the new, renewal, or continuing approval is issued on January 1, it will have an expiration date December 31. If an addendum is approved during this time, the approval still last only until December 31. Please incorporate all modifications and addendums into the renewal application, protocol, and when applicable the informed consent forms for the IRB consideration during the annual review.
- Changes will be reviewed by the IRB at the next available meeting.
- Please include a cover letter explaining the requested modifications, and any modified items such as consent forms, protocols, Investigator Brochures, study instruments, recruitment tools, etc.
- When changing Investigators, please include a new signed site submission form from the new Investigator accepting responsibility for the research. Changes in Investigators usually qualify for expedited review.

### **Protocol Deviations**

Alpha IRB requires that all significant protocol deviations be reported. In general, significant deviations are considered to be protocol deviations that:

- adversely affect the safety, rights or welfare of subjects or others
- adversely affect the integrity of the study data
- have or might occur again (if it is anticipated that this violation will occur again, an amendment to the protocol should be considered)

Significant protocol deviations need to be reported to Alpha IRB promptly, but no later than **ten (10) business days** from the date the site became aware of the event.

### **Continuing Review/Study Completion**

- **Study Renewal**

Reports must be submitted by the investigator and/or study sponsor at

intervals determined by the IRB. The expiration date and the date that an interim report is due, if required, will be stated in the study approval letter. Reminders will be sent to the Investigator and to the Sponsor prior to the due date.

The Federal regulations do not allow an IRB to approve a study for more than one year. For multi-year research, the Principal Investigator is responsible for submitting a renewal application prior to the expiration of the current IRB approval.

If the approval expires prior to submission of the renewal application, the investigator is required to suspend subject contact and data collection until the renewal is approved by the IRB. For therapeutic studies where subject safety is a concern, there is some flexibility towards the continued treatment for currently enrolled subjects. However, no new subjects may be contacted, recruited, or enrolled until the Investigator obtains current IRB approval.

The renewal application should incorporate all of the addenda and modifications submitted to and approved by the IRB during the previous approval periods.

Continuing review and approval is necessary if recruitment of subject's stops but previously enrolled subjects continue to participate in the research or the study is in data analysis.

Reports must be submitted by the Investigator at intervals determined by the IRB. The expiration date and the date that an interim report is due, if required, will be stated in the study approval letter. A reminder will be sent to the Investigator prior to the due date.

- **Completion/Termination**

In order to formally complete a study file, the IRB requests that Investigators officially notify the IRB when a study is terminated or completed or after data analysis is complete and submit the Continuing Review/Close-Out Report when closing out a study.

## **Monitoring Reports**

As sponsors routinely monitor investigative sites, they are in a unique position to uncover information to which the IRB may not otherwise have privy. The Investigator should request that the sponsor provide any information that may affect the rights and welfare of participants, or their willingness to continue participation. Such information may be contained within a monitoring report, or may be summary of the sponsor's assessment. The Investigator will then notify the IRB of these findings.

## **REPORTS OR COMPLAINTS FROM EMPLOYEES, STAFF AND SUBJECTS**

Alpha IRB encourages sponsors, investigators and research staff to contact us with any feedback, suggestions, or concerns related to the protection of human subjects or IRB processes. You may contact Alpha IRB at 949-542-3882 or email at: [info@alphairb.com](mailto:info@alphairb.com).

## **Additional Information**

### **Resource List**

Food and Drug Administration – [www.fda.gov](http://www.fda.gov)

United States Department of Health & Human Services – [www.hhs.gov](http://www.hhs.gov)

The World Medical Association – [www.wma.net](http://www.wma.net)

Frontiers in Bioscience – [www.bioscience.org](http://www.bioscience.org)

ACRP – [www.acrpnet.org](http://www.acrpnet.org)

CITI Collaborative Institutional Training Initiative – [www.citiprogram.org](http://www.citiprogram.org)

Medical Device Link – [www.devicelink.com](http://www.devicelink.com)

### **Alpha Independent Review Board**

1001 Avenida Pico, Suite C #497

San Clemente, CA 92673

P: 949-542-3882

F: 949-940-0134

[www.alphairb.com](http://www.alphairb.com)

**OHRP Number: IORG005158/ IRB00006205**