

ARGUS IRB, INC.
STANDARD OPERATING PROCEDURES

**6668 S. HIDDEN FLOWER WAY
TUCSON, AZ 85756-5111**

PHONE (520) 298-7494

FAX (520) 298-7494

JUNE 2010

ARGUS IRB
STANDARD OPERATING PROCEDURES
TABLE OF CONTENTS

Section 1	Basic Charter
Section 2	Purpose and Functions of the IRB
Section 3	IRB Membership
Section 4	IRB Operation
Section 5	IRB Records
Section 6	Informed Consent
Section 7	Amendments/Changes to Standard Operating Procedures
Section 8	Medical Devices
Section 9	Financial Compensation for Board Members
Appendix A	IRB Meeting Attendance Log
Appendix B	Ongoing Review/Report to IRB
Appendix C	Final Report to IRB

Section 1: Basic Charter

- 1) It is the policy of Argus IRB Inc. (hereafter “Argus” or “the company”) that all research involving human subjects meets high professional and ethical standards. In accordance with this policy, the company has established the Argus Independent Review Board (“IRB” or “the Board”). The IRB will base its examination of proposed research on the following principals:
 - i) Protection of the safety, rights and dignity of human research subjects and assurance of high ethical standards for all research involving human subjects.
 - ii) Assurance that the quality of the scientific base warrants exposure of the human subjects to the risks of the proposed research.
 - iii) Helping to assure that applicable laws and government regulations are fully complied with.
- 2) In order to fulfill its responsibilities, the IRB will adhere to the Standard Operating Procedures detailed in the remainder of this document.

Section 2: Purpose and Functions of the IRB

- 1) The Argus IRB shall:
 - i) Have a primary responsibility of protecting human subjects from undue risk and assuring that the personal rights and dignity of human subjects are upheld.
 - ii) Determine if the potential risks to human subjects in proposed research studies are reasonable and if the anticipated benefits to the subjects and/or knowledge to be gained are sufficient to warrant approval of human subject participation.
 - iii) Assure that subject participation is voluntary, as documented by written informed consent, and that informed consent is obtained from each subject by adequate and appropriate methods.
 - iv) Conduct reviews with objectivity and in a manner to ensure the exercise of independent judgment by its members.
 - v) Bring to bear its collective experience as well as individual expertise and diverse backgrounds in reviewing each proposal and requesting additional information, such as specific data, whenever necessary for clarification before a final decision is rendered.
 - vi) Approve protocols and consent forms as submitted, require modifications before approval or disapprove proposed research in order to fulfill the responsibilities of the IRB as stated above.

Section 3: IRB Membership

- 1) The IRB shall be composed of at least five, but no more than ten, members with different backgrounds to promote a complete and adequate review of research activities conducted at Argus.
- 2) The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the member's backgrounds, including consideration of the racial and cultural backgrounds of members, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.
- 3) The IRB may not consist entirely of men, women or members of one profession.
- 4) The IRB shall include at least one member whose primary expertise and/or concerns in nonscientific areas, such as a lawyer, member of the clergy, or a housewife.
- 5) No IRB member may be an employee of a research company.
- 6) **IRB Chairperson** – The Chairperson will be chosen by a majority vote of all IRB members once yearly at the IRB business meeting and will be the presiding officer at all IRB meetings. Duties and functions of the Chairperson will include:
 - i) Taking minutes at all Board meetings. The minutes will also include notification of the action taken by the Board with respect to the protocol being considered and will be signed by the Chairperson. The Chairperson has the option of appointing a Board member to serve as acting Chairperson if the Chairperson is unable to attend a protocol review meeting.
 - ii) Maintaining complete records of all IRB activities, including protocols considered by the IRB, consent forms, the minutes of all meetings, correspondence, etc. (see Section 5).
 - iii) Conducting expedited reviews of new protocols or approving minor protocol changes when appropriate. The Chairperson may also designate two board members to conduct expedited reviews or approve minor protocol changes, but the Chairperson will be responsible for communicating the results of such a review to the Principal Investigator.
- 7) **Selection, Term of Service, Removal of Board Members and Chairperson** – Potential Board members may be recommended by the Chairperson or Board members and require approval by the Board. No specific term of service is stipulated for Board members. The Chairperson will serve a term of 1 year and with the required Board vote, may serve as many consecutive terms as he/she desires. The President of Argus IRB INC. may remove board members from service at his/her discretion.

Section 4: IRB Operation

Part 1 **Meeting Frequency/Location** – Meetings of the Board will be scheduled on an as-needed basis (but at least once per year). Board meetings will be held at Argus IRB, 6668 S. Hidden Flower Way, in Tucson, Arizona. A record of Board members present at each meeting will be kept by the Chairperson. If possible, Board members will be notified at least 2 weeks prior to the meeting date.

Part 2 **Quorum Requirements** – A quorum consisting of a simple majority of the Board members is required.

Part 3 **Procedures for Initial Review of a Proposed Study** – To enable the Board to review a proposal promptly and thoroughly, the Principal Investigator will submit to all Board members copies of the study protocol, consent form and any other pertinent information at least two weeks prior to the meeting, if possible. Board members will study the protocol prior to the meeting and be prepared to discuss it at the meeting. During the meeting, the Board will review the protocol and consent form and discuss any questions or concerns they may have. The Principal Investigator and Vice President/Technical Directive will be available to answer any questions or concerns Board members may have, although he/they will only be present in the meeting room when requested by the Chair.

Part 4 **Criteria For Approval of a Proposed Study** – The Board may approve a proposed study only after it has determined that all of the following requirements will be met:

1. Risks to human subjects are reasonable in relation to anticipated benefits, if any, to subjects and the importance of the knowledge that may be expected to result.
2. Risks will be minimized by:
 - i. Using procedures that are consistent with sound research design and which do not expose subjects to risk unnecessarily.
 - ii. Using procedures, whenever appropriate, which are already being performed on the subjects for diagnostic or treatment purposes.
 - iii. Insuring that subject participation will be voluntary as documented by written informed consent obtained from each subject by appropriate methods.
 - iv. Where appropriate, the protocol contains adequate provisions for monitoring accumulating data to ensure the safety of subjects.
 - v. Selection of subjects will be equitable, considering the purposes of the research and setting in which the research will be conducted.
 - vi. Where appropriate, there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of data.

- vii. If some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as persons with acute or severe physical or mental illness, or persons who are economically or educationally disadvantaged, the IRB will determine if appropriate additional safeguards are needed to protect the rights and welfare of these subjects and, if so, will require that safeguards are included in the study.

Part 5 **Criteria For Disapproval of a Proposed Study** – The IRB may disapprove a protocol if one or more of the above conditions for approval are not met or if the Board determines that:

1. Data or other information submitted to the Board contains inaccurate or misleading statements.
2. Information necessary for the Board to fully evaluate a proposal is deliberately withheld from the Board.
3. The Principal Investigator's scientific qualifications or the medical support/clinical laboratory are inadequate to insure proper conduct of the study.

Part 6 **Procedures For Board Action** – On the basis of a simple majority vote of the Board members present at the meeting, the Board may take the following action:

1. Approve the protocol/consent form as written. In this case, the Principal Investigator will be notified in writing by the IRB Chair.
2. Approve the protocol/consent form after one or more amendments or modifications. The Principal Investigator will be notified of the required modifications in writing by the IRB Chair. The Principal Investigator will then resubmit an amended protocol/consent form, and a written explanation of each change made, to the Chairperson.

If the revised protocol/consent form meets the requirements set forth by the Board, the Chair may approve for the Board and notify the Principal Investigator in writing.

If any changes are made in the protocol/consent form in addition to those required by the Board, such changes will also be included in the written explanation. In general, such changes should be limited to spelling, grammar or other minor changes so that the revised protocol/consent form continues to meet the criteria for approval set forth in Section 4, Part 4 above.

If more substantial changes are made, the Chair will notify the Principal Investigator that such changes will require another meeting of the Board. If the Principal Investigator still wants the substantial changes to be included, the Chair will call another meeting of the Board.

If the revised protocol/consent form does not meet the requirements of the Board, the Chair will notify the Principal Investigator in writing of the need

for further revision and the Principal Investigator may then make the needed changes and resubmit to the Chairperson.

The Chairperson will not require amendments or modifications in addition to those required by the Board at its meeting concerning the protocol, except on the basis of new information about the study/drug as provided in Section 4 Part 8.6.

3. Disapproval the protocol/consent form. The rationale for such a decision will be stated in writing and the Principal Investigator will be given an opportunity to respond to the Board in person or in writing. As a result of the Principal Investigator's response, the Board may elect to approve, approve after changes, or continue to disapprove the study.

Part 7

Procedures For Expedited Review – The following procedures have been established for expedited IRB review of protocols involving minimal risk to subjects or protocol changes in previously approved studies.

1. Review of minimal risk protocols or proposed minor changes in previously approved clinical studies may be conducted by the Chair or two experienced Board members designated by the Chair.
2. The Chairperson or designated reviewers may a) approve the protocol or the changes if the revised protocol meets the criteria for approval set forth in Section 4, Part 4 above, b) request further protocol/consent form changes, or c) refer the protocol to the Board for full review.
3. The Chairperson or designated reviewers may not disapprove a protocol/consent form under the expedited procedure. A proposed study may be disapproved only by a meeting of the full IRB.
4. Board members will be advised of research proposals which have been approved by expedited review at the first full Board meeting following approval of the research and such information will be included in the minutes of the meeting, which will be mailed to all Board members.

Part 8

Continuing Review of IRB Approval Studies – The Board will insure that there is adequate follow-up of IRB-approved studies. This continuing review procedure is designed to make sure that the study was carried out using the protocol/consent form approved by the IRB.

1. A study approved by the IRB will be reviewed at least once a year by the IRB Chair unless a more frequent review is required by the Board at the initial review of the study. Based upon this review, the Chair may give approval for continuation of the study. If the Chair determines a meeting of the Board is required for approval to continue the study s(he) has the authority to call such a meeting.
2. The Board will consider the degree of risk involved in a study when determining the frequency of review it will require.

3. After a study is approved and enrollment begins, the Principal Investigator or his designee will send to the Chairperson a copy of the consent form signed by the first subject enrolled in the study.
4. The Principal Investigator will inform the Chair in writing if a study is terminated prior to completion. Such notification will also include the reason(s) for termination of the study. The Board will be informed at the next meeting.
5. Serious adverse experiences, including those causing syncope, cardiopulmonary arrest, arrhythmia, substantive liver or kidney function changes, drug overdose, cancer, psychosis, permanent disability, hospitalization or death will be reported immediately to the IRB chairperson and the study sponsor by telephone, with a written follow up within five working days. Minor adverse experiences will be noted in the final report.
6. The Principal Investigator will keep the Board informed of new information regarding the safety of drugs being used in IRB approved studies.
7. An Interim Report form will be sent to the IRB Chair at intervals specified by the Board, or at least annually.
8. A final report will be sent to all IRB members after completion of a study.

Part 9

Suspension or Termination of IRB Approval –

1. The IRB shall have authority to suspend or terminate approval of research that 1) is not being conducted in accordance with the IRB's requirements, or 2) has been associated with unexpected serious harm to subjects.
2. In the event the IRB chooses to suspend or terminate a research project, the Chairperson will notify the Principal Investigator of this decision both verbally and in writing.
3. Any such suspension or termination of approval shall include a statement of the reasons for the Board's action.

Section 5: IRB Records

1. The IRB shall maintain adequate documentation of all IRB activities. It will be the responsibility of the IRB Chairperson to maintain IRB records.
2. IRB records will include the following:
 - (1) Copies of all research proposals reviewed, scientific evaluations (if any) that accompany the proposals, consent forms, study initiation forms, progress reports, adverse event reports, and final reports.
 - (2) Minutes of all IRB meetings. These shall be in sufficient detail to show attendance at the meetings; actions taken by the Board; the vote on these actions, including the number of members voting for, against and abstaining; and the basis for requiring changes in or disapproving research.
 - (3) Records of continuing review activities.
 - (4) Copies of all correspondence between the IRB and the investigators.
 - (5) A list of IRB members identified by name, earned degrees, and experience (such as board certifications, licenses, etc.) sufficient to describe each member's chief anticipated contribution to the Board's deliberations.
 - (6) Written procedures for the IRB.
 - (7) Statements of significant new findings provided to subjects.
3. The records outlined above shall be retained for at least 3 years after completion of the research, and shall be accessible for inspection and copying by authorized representatives of the Food and Drug Administration at reasonable times and in a reasonable manner.

Section 6: Informed Consent

1. Informed consent must be obtained from all subjects prior to enrollment in any study conducted by Argus.
2. The IRB shall require that information given to subjects as part of informed consent is in accordance with Part 50, Section 50.25 of the Code of Federal Regulations. Specifically, informed consent must contain the following elements:
 - (1) A statement that the study involves research and an explanation of the purposes of the research.
 - (2) The expected duration of the subject's participation in the research project.
 - (3) A description of the procedures to be followed and identification of any procedures which are experimental.
 - (4) A description of any reasonably foreseeable risks or discomforts to the subject.
 - (5) A description of any benefits to the subject or others which might reasonably be expected from the research.
 - (6) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
 - (7) An explanation of whom to contact for answers to questions about the research-related injury to the subject.
 - (8) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the patient is otherwise entitled.
 - (9) A statement that medical treatment will be available if study-related injury occurs.
 - (10) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.
 - (11) A description of all information concerning payment to research subjects, including the amount and time of payment.
3. When appropriate, one or more of the following elements of informed consent shall also be provided to each subject.

A statement that identifies the drug to be used in the study, its therapeutic class and, when appropriate, a statement that the subject may receive either active drug or placebo.

A statement that there may be risks to the subject which are currently unforeseeable.

Argus IRB Standard Operating Procedures

A statement that the investigator may remove individual subjects from the study, with or without the consent of the subject.

For extended studies, a statement that significant new findings developed during the course of the research which may affect the subject's willingness to continue participation will be provided to the subject.

A statement that females of childbearing potential must agree to use birth control during the study.

A statement that pregnant or nursing females will be excluded from the study.

Section 7: Amendments/Changes to Standard Operating Procedures

1. The Board may elect to amend or change these standard operating procedures.
2. All Board members will be advised by the Chairperson in writing of proposed amendments or changes to these standard operating procedures. At the next Board meeting, proposed amendments and changes will be discussed and may be approved by a two-thirds majority of those present. Any Board member may also present amendments or changes to these standard operating procedures. Proposed amendments and changes will be discussed and may be approved by a two-thirds majority of those present.

Section 8: Medical Devices

Clinical investigations undertaken to develop safety and effectiveness data for medical devices must be conducted according to the requirements of the IDE regulations found in 21 CFR 812.

Certain research studies of devices may be exempt from IDE regulations (e.g., marketed devices). If the device is not exempt from IDE regulations, the device must be categorized as either “significant risk” (SR) or “non-significant risk” (NSR).

The Sponsor initially determines the risk category of the device. The proposed study is then submitted to FDA (SR studies) for approval. SR and NSR studies are then reviewed by the IRB prior to the initiation of any study-related activities.

The Sponsor must prepare and submit a Risk Assessment Report explaining the device classification. 21 CFR 812.150(b)(10).

The IRB will also use information from the project descriptors, protocol, the Investigator’s Brochure, package insert, FDA Information Sheets, reports of prior investigations conducted with the device, description of subject selection criteria, monitoring procedures and other evaluations presented by the Sponsor to categorize the device as “SR” or “NSR”.

Argus may disagree with a sponsor or investigator’s classification of the device as NSR. If so, the investigation cannot proceed until both the IRB and FDA approve the investigation. The FDA has the ultimate decision in determining if a device is SR or NSR.

PROCEDURES

1. The IRB (or FDA) will determine whether the medical device is “Significant Risk” (SR) or Non-significant Risk (NSR) per 21 CFR 812 by use of the following:
 - a. A “Risk Assessment Report” from the sponsor explaining the device classification
 - b. FDA letter approving the IDE or a 510K clearance
 - c. A Pre-Market Approval letter, supplement letter or amendment letter from FDA
 - d. Use of information from the project descriptors, protocol, investigator’s brochure (or package insert) and other risk evaluations presented by the applicant (Sponsor, Investigator, etc.).
 - e. Review of the FDA Information Sheet located at:
<http://www.fda.gov/oc/ohrt/irbs/devices.html#risk>
 - f. Reports of prior investigations conducted with the device
 - g. Description of subject selection criteria
 - h. Description of monitoring procedures

- i. Other evaluations presented by the sponsor
- j. Definitions to be used by ARGUS IRB in SR / NSR determinations:
 - i. A SR device study is defined as the study of a device that presents a potential for serious risk to the health, safety or welfare of a subject and
 - (1) is intended as an implant; or
 - (2) is used in supporting or sustaining human life; or
 - (3) is of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise prevents impairment of human health; or
 - (4) otherwise presents a potential for serious risk to health; safety and welfare of a subject.
 - ii. Device studies submitted to the IRB for review with an approved IDE will be considered SR studies. A NSR device study is one that does not meet the definition for a significant risk study. IF the FDA determines that a device is a NSR device, the IRB will accept FDA's determination.
- k. In addition to the above, the IRB shall consider the proposed use of the device and the nature of harm that may result from its use in the study. Studies in which the device used poses a potential harm to subjects that could be life threatening, result in permanent disability or impairment of a body function or part, or necessitate medical or surgical intervention to preclude permanent impairment of a body function or part, will be considered to involve SR devices.
- l. For NSR device studies, the IRB shall proceed to review the study per 21 CFR 56.111. If approved by the IRB, the investigator must comply with all abbreviated IDE requirements in 21 CFR 812.2(b), as well as informed consent and IRB regulations.
- m. All SR studies are considered more than minimal risk and require full IRB review.
- n. If the IRB decides the study is Significant Risk, the IRB shall notify the investigator (in writing) that they must obtain an IDE from the FDA prior to IRB review of the study. Any amendments or corrections of deficiencies required by FDA during the IDE process must be submitted for review and approval of the IRB.
- o. If an IDE application is or has been submitted to FDA, but final approval has not been granted, the IRB can proceed with the review of the study, but final approval will not be granted until documentation of the FDA approval is submitted.
- p. Once the IDE is obtained, the sponsor / investigator may resubmit the study to the IRB for review.
- q. The IRB will review reports of unanticipated device effects. Investigators are required to report these events to the IRB within 10 working days of their receipt of the information. Should the IRB determine that the information gained in these reports changes the risk assessment; the IRB can reconsider any NSR decision and / or require the modification of the informed consent to contain the new information.
- r. A copy of this correspondence will be kept in the IRB files for the study

Section 9: Financial Compensation for Board Members

1. Each member in attendance and participating in the review of a protocol/consent form submitted to the Board will receive compensation per protocol/consent form reviewed. Board members will not be compensated for review of a protocol/consent form if they do not attend the meeting for that study.
2. The Chairperson will receive compensation for each protocol/consent form reviewed.
3. Expedited Reviews – The following fees will apply to protocols/consent forms reviewed under the expedited review procedures (Section 4, Part 7, this document).
 - (1) The Chairperson and/or other Board members participating in an expedited review of protocol/consent form will receive compensation.
 - (2) If, as a result of an expedited review, the protocol/consent form is referred to the full Board for review at a Board meeting, the Chairperson and/or other Board members participating in the original expedited review will not be paid again for that protocol/consent form. Board members who were not participants in the original expedited review, but who attend the subsequent full review meeting will, of course, be paid the normal amounts as in Section 8.1-8.2 above.
4. The Board will conduct a business meeting once a year at a date and time to be set by the Board.

Appendix A – IRB Meeting Attendance Log

Date:

Protocol Reviewed:

Present:

1.

2.

3.

4.

5.

6.

7.

8.

9.

10.

Appendix B - Ongoing Review/Report to IRB

Date:

Study Title:

Protocol #:

Protocol Date:

Amendment Date(s):

IRB Approval Date(s):

Date First Subject Enrolled:

Total Number of Subjects Enrolled:

Total Number of Dropouts:

Reasons for Dropouts:

Total Number Discontinued:

Reason(s) for Discontinuation:

List Adverse Events/Severity/Outcome:

List Any New Findings:

Next/Final Report Due:

Appendix C – Final Report to IRB

Date:

Study Title:

Protocol #:

Protocol Date:

Amendment Date(s):

IRB Approval Date(s):

Date First Subject Enrolled:

Total Number of Subjects Enrolled:

Total Number of Dropouts:

Reasons for Dropouts:

Total Number Discontinued:

Reason(s) for Discontinuation:

Total Number of Subjects Completing Study:

Date of Close-out Visit:

Results of Study:

Adverse Event(s) Summary: