SONORAN UNIVERSITY
OF HEALTH SCIENCES

Clinical Research Policy Manual
Institutional Review Board (IRB)

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1. Clinical human research at Sonoran

A. Introduction

Sonoran University of Health Sciences (Sonoran) is committed to protecting the rights and welfare of its volunteer research subjects enrolled in clinical research trials at Sonoran and the Southwest Naturopathic Medical Center (SNMC). The Assurance of Compliance and this policy manual are written to comply with ethical and legal requirements for the conduct and oversight of clinical human research.

The Institutional Review Board (IRB) is an independent review committee designed to oversee the conduct of clinical research at Sonoran.

I. Definitions

The following definitions are used in this Sonoran Policy manual.

- "Research" means a systematic investigation, including research development, testing and evaluation, designed to contribute to generalizable knowledge. (45 CFR 46.102 (d)).
- “Human Subject " means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. Some clinical and basic research activities with human tissues (i.e., blood and tissue samples, etc.) may also constitute research with human subjects. (45 CFR 46.102 (f)).
- Clinical Trial as defined by the National Institutes of Health (NIH, 45 CFR 46)
- A biomedical or behavioral research study of human subjects designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new biomedical or behavioral interventions are safe, efficacious, and effective. Clinical trials of an experimental drug, treatment, device, or intervention may proceed through four phases:

Phase I. Testing in a small group of people (e.g. 20-80) to determine efficacy and evaluate safety (e.g., determine a safe dosage range and identify side effects).

Phase II. Study in a larger group of people (several hundred) to determine efficacy and further evaluate safety.

Phase III. Study to determine efficacy in large groups of people (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions, to monitor adverse effects, and to collect information to allow safe use.

Phase IV. Studies done after the intervention has been marketed. These studies are designed to monitor the effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use.

- Clinical Investigation as defined by the Food and Drug Administration (FDA) (21 CFR 56.102(c))
- Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or need not meet the

requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part.

- "Collaboration " exists if a Sonoran participant expects "something in return" as a result of having participated in a research activity. "Something in return" could include data, authorship on a publication, samples, or even patent rights. Sonoran views authorship as prima facie evidence of collaboration. Collaborative activities may include but are not limited to the collection of specimens, visits to institutions to perform research activities or clinical work, exchange of information containing personal identifiers, preliminary data-collection activities involving human subjects, and substantive intellectual contributions to research techniques, protocol design, or interpretation of data. Even remote participation--such as supplying important reagents, performing tests, or analyzing data--may constitute collaboration. Not all collaborations are defined in advance, and there may be subsequent differences of opinion about whether collaboration existed or perhaps developed during the course of research activities. In unclear cases, investigators should contact the Sonoran IRB Chair. In some cases further objective third-party review may be necessary.

II. Applicability

a. This Assurance is applicable to all research activities that, in whole or part, involve human subjects if:
   - the research is conducted or supported by Sonoran, or
   - the research is conducted by any employee of Sonoran in connection with his/her institutional duties, regardless of the site of the activity, or
   - the research is conducted in a facility of Sonoran or SNMC, or
   - the research involves the use of any of Sonoran/SNMC non-public information systems or databases to identify or contact human subjects or prospective subjects or access medical information.

b. Certain cooperative research, including research conducted at Southwest Naturopathic Medical Center, will be conducted in accordance with this policy manual.

c. Activities in which the only involvement of human subjects is in one or more of the categories listed in 45 CFR 46.101(b) are exempt from coverage under this Assurance.

B. General Institutional Policies

i. It is the policy of Sonoran to respect and safeguard the rights and welfare of human subjects involved in its research activities.

ii. Sonoran acknowledges that it bears responsibility for the performance of all research involving human subjects covered by this policy manual, including continuing compliance with pertinent federal, state or local laws, as they may relate to such research.

iii. Sonoran ensures that SNMC director, Sonoran IRB Chair, and all researchers engaged in the planning, conduct and program oversight of research involving human subjects complete the required human subjects protection training as described in the Sonoran policies and procedures.

iv. Sonoran ensures that the SNMC Chief Medical Director and Research Advisory Board members complete the required human subjects protection training as described in the Sonoran policies and procedures.
v. Sonoran ensures that Sonoran IRB members and alternate members complete the required human subjects protection training as described in the Sonoran policies and procedures.
vi. Sonoran ensures that Sonoran Principal Investigators (PI) and non-Sonoran PIs submitting human subjects research to the Sonoran IRB for review complete the required human subjects protection training as described in the Sonoran policies and procedures. Co-investigators, administrators, research assistants and independent contractors are also required to complete the required human subjects protection training as stated in the Sonoran policies and procedures for research.
vii. It is the policy of Sonoran that Sonoran IRB will review only research which has been reviewed by the Research Advisory Board (RAB) and found to be scientifically meritorious, well-designed, and in keeping with ethical guidelines, program relevance and public responsibility.
viii. The Medical Director, acting on behalf of Sonoran, is responsible for implementation of the Sonoran Assurance of Compliance (Sonoran AC). The Sonoran AC authorizes policies and procedures, and provides education, guidance and assistance to Sonoran IRB, Sonoran research investigators and others in conducting human subjects research, and other Sonoran officials in conformance with the terms and conditions of the Sonoran AC and federal regulations (45 CFR 46, 21 CFR 50, 56).
ix. Sonoran establishes and maintains the Institutional Review Board (IRB). The IRB is responsible for the prospective review and approval of research activities involving human subjects. Their primary mandate is to protect the rights and welfare of human research subjects. The composition and operation of each IRB will conform to the terms and conditions of 45 CFR 46 and 21 CFR 50, 56 (where applicable).
x. Activities in which the only involvement of human subjects is in one or more of the categories listed in 45 CFR 46.101(b) will be submitted by Sonoran researchers to the Sonoran IRB for determination and documentation of exemption from the requirement for IRB review and approval.
xi. It is the policy of Sonoran that, except for those categories of research determined to be exempt from the requirement for IRB review and approval, no research activity covered by this policy manual will begin before:
    a. it has been reviewed and approved by the Research Advisory Board and IRB,
    b. completion of required training by the Principal Investigator,
xii. the informed consent of the subject or the subject's legally authorized representative has been obtained, unless this requirement has been altered or waived by an IRB in accord with 45 CFR 46.116(d) and 21CFR 50.23 or 24, and
xiii. IRB review and approval has been documented so that it may be entered into an appropriate Sonoran location.
xiv. Sonoran will provide appropriate additional safeguards in research that involves: (1) pregnant women (see 45 CFR 46 Subpart B), (2) Native Americans, (3) children (see 45 CFR 46 Subpart D), (4) the cognitively impaired, or (5) other potentially vulnerable subjects such as those who are economically or educationally disadvantaged.
xv. As a means of safeguarding the rights and welfare of human subjects, Sonoran will encourage continuing constructive communication and education among the Sonoran IRB, Research Advisory Board, principal investigators, clinical care staff, administrative personnel, and other institutional officials and research subjects.

xvi. When research is conducted in the Sonoran clinical sites, short-term medical care will be provided for injury resulting from participation in research.
xvii. Sonoran will provide appropriate resources to the IRB to assure proper functioning and record- keeping in conformance with the Sonoran AC and 45 CFR 46.
xviii. Sonoran will periodically assess IRBs' practices, procedures and record-keeping.
xix. Sonoran official will be made available to Sonoran investigators and personnel conducting and/or reviewing human subjects research activities.
xx. Sonoran will adhere to the guidelines set forth in the May, 1991 Office for Protection from Research Risks (OPRR) Reports, "Emergency Medical Care".
xxi. Sonoran will adhere to applicable DHHS Policies regarding HIV research.
xxii. Sonoran will adhere to "The Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research." (59 Federal Register 11146-11151, effective March 9, 1994.)

C. Scope of research program

Southwest College of Naturopathic Medicine conducts research in keeping with the mission of the College. This may include but is not limited to research regarding naturopathic medicine, naturopathic modalities, clinical practices and medical education. Research may include analysis of medical substances, devices and drugs.

Sonoran does not support or oversee research that is not designed to support the health and well- being of the population. Products marketed for frivolous or unhealthful purposes are not supported by the Sonoran research program. Southwest College does not support research on prisoners.

2. Compliance

A. Federal compliance

The basic legal principles governing human subject research, covered by the AC and applicable to individual protocols are:

- Federal Policy for Protection of Human Subjects (Common Rule) in 45 CFR Part 46
- Food and Drug Administration Regulations for the Protection of Human Subjects in 21 CFR Parts 50 and 56
- Standards for Privacy of Individually Identifiable Health Information (HIPAA Privacy Rule) in 45 CFR Parts 160 and 164.
- Department of Veterans Affairs regulations in 38 CFR Part 16 and VHA Handbook 1200.5
- Applicable Arizona law and other legal and ethical guidelines where appropriate
- AZ naturopathic physician licensure statutes
- The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research.
- The Nuremberg Code
- The Helsinki Declaration

The regulations in 45 CFR 46 Subpart A will be applied to all non-exempt Human Research, regardless of the source of funding.

B. Assurance of Compliance

Recorded with the Office of Human Research Protections (OHRP) FWA#: FWA00000437
IORG #: IORG0000481 IRB00000803

3. Institutional policies

A. IRB/RAB

I. Responsibilities

- The Institutional Review Board (IRB) serves to protect the rights, well-being, and personal privacy of volunteers participating in research studies at or involving any Sonoran facilities. The IRB insures a favorable, ethical climate for conduct of scientific inquiry and protects the interests of Sonoran.
- These policies and procedures apply to all research involving human beings at Sonoran regardless of the source of funding for such research. The IRB and Sonoran are responsible to communicate the policies of Sonoran to existing or potential scientific investigators or personnel.
- Appropriate professional attention and facilities shall be provided to insure the safety and well-being of human subjects. No subject in a research activity is to be exposed to unreasonable risk to health or well-being.
- Research involving people under the age of 18 years, other people considered legally incompetent, and people unable to give informed consent may be approved if there is no unreasonable risk or suffering for the individual subject and if the potential benefits far outweigh the potential risks. Sonoran does not conduct research involving prisoners.
- The confidentiality of information received from subjects in experiments or respondents to questionnaires will be fully protected, both during and after the conduct of any research activity, within the limits of the law. This includes protecting the confidentiality of information in electronic or any other information storage and retrieval format.
- Consent- Before a subject participates in research involving risk or substantial stress or discomfort, the exact nature of the risk will be carefully and completely explained. The investigator will be satisfied that the explanation has been understood by the subject. The voluntary consent of the research subject will be obtained after complete disclosure and a period of time in which the subject can ask any and all questions. Other elements of informed consent are established by the Federal government, international convention, Sonoran, and the IRB.
- A request by any subject for withdrawal from a research activity shall be honored promptly without penalty and without loss of benefits to which the subject is otherwise entitled, within the limits of the research.
- The IRB follows regulations of the DHHS and FDA(45 CFR 46.107 and 21 CFR 56.107).

II. Research Advisory Board (RAB)

The Research Advisory Board will conduct a scientific merit review of all applications prior to submission to the IRB for approval from a human subjects safety perspective. Frivolous or poorly designed studies and out-of-date research methods can endanger human subjects' safety and therefore a scientific merit review is required to screen for these problems.

III. Membership of the IRB

Sonoran will maintain an IRB constituted to comply with the assurance and federal regulations. In accord with these regulations, a majority of members of the IRB must be present to constitute a quorum, and one of those present must be a member whose primary concerns are in

nonscientific areas. Normally the IRB is composed of faculty members, and a member who is not otherwise affiliated with Sonoran and who is not part of the immediate family of a person affiliated with Sonoran. A student representative may attend. The number of IRB members can be expanded or contracted to suit the workload of the IRB, provided it has at least five members and otherwise fulfills federal requirements. At Sonoran, the IRB membership includes at least 2 clinical ND faculty members and 2 basic sciences PhD or MD/PhD faculty members to ensure a diversity of opinion and expertise. More than the minimum number of members from each category may serve on the IRB, however only a majority of members as noted must be present at any meeting to constitute a quorum.

Alternate members of the IRB may be named to insure a quorum at any regularly scheduled IRB meeting. If a member finds it necessary to be absent from one or more meetings, the member will notify the Chair to that effect so that an alternate member can serve in the place of the absentee
.
The Chair reports back to the Faculty Senate as required or requested by the President of the Faculty Senate. The IRB is self- perpetuating. Current members nominate and vote to elect new members by simple majority. Each board member has one vote. The Chair may only vote in the event of a tie.

If the IRB begins to regularly review research that involves a vulnerable category of subjects (45 CFR 46.205-409), consideration will be given to inclusion of one or more individuals who have special knowledge, expertise, and experience in working with these subjects.

IV Conflict of interest

If any member has an interest (as investigator, financially, or otherwise) or the appearance of an interest in an application to be reviewed by the IRB, the member will tell the Chair of the situation and recuse himself or herself. The member is not allowed to be present during discussion, does not count toward the quorum for the vote, and is not allowed to vote on the proposal. If the Chair or any other IRB member feels that a member has an interest or appearance of an interest, they may ask the Chair to ask the member to recuse himself or herself.

V. Procedures for Application Review

The application will be submitted to the RAB (Research Advisory Board) for scientific merit review. Once the suggestions of the RAB have been made and approved, the application will be submitted to the IRB chair.

Each applicant must complete and submit an application form approved by the IRB, one hard copy with official signature and electronic copy. Each application will be given an initial review by the Chair to insure that it is complete, meets all IRB requirements, and is of acceptable quality. If the Chair chooses, the application can be returned with requests for improvement to meet minimum IRB standards without a review, or may be denied without review.

An investigator with an application pending before the IRB is required to be available at the meeting where the application is to be reviewed, or to have a designated agent available, should the IRB have questions for him or her. Additionally, an investigator may, at the Chair's discretion, attend the portion of the meeting

set aside by the Chair for the investigator's appearance. However, the investigator is not allowed to be present during discussion of or the final vote on the application.

The Chair will notify the investigator and the institution of any decision on an application, in writing, including reasons for disapproval or requirement of notification in the event of these. The IRB will give the investigator the opportunity to respond in person or in writing.

Each investigator will submit a signed investigator assurance form (PI responsibilities) with each application agreeing to promptly report to the IRB any proposed changes in the approved research, any unanticipated problems involving the risk to subjects or others, and incidents of adverse events (anticipated or otherwise). The investigator agrees not to initiate changes until approved by the IRB except when necessary to eliminate apparent, immediate hazards to subjects. The investigator agrees to provide immediate notification (within 48 hours) of serious anticipated or unanticipated adverse events.

Each application accepted by the Chair will be assigned to a primary reviewer. The Chair may serve as a primary reviewer. The primary investigator is responsible for summarizing the application (human subject safety issues) for the IRB. All IRB members are expected to read the application in its entirety prior to the meeting where it is discussed. The final IRB decision on each application will be by a majority vote of the members present after the primary investigator's presentation and a discussion moderated by the Chair. If desired, any IRB member may ask any vote to be conducted by ballot to conceal the identity of each voter from other IRB members, though the Chair must always know the vote of each member of the IRB and is responsible to determine the outcome of the vote (no true anonymous voting is allowed).

- Risk categories
  - After the vote is taken, the IRB will determine if the protocol merits low, medium or high risk.
  - Low risk studies involve no impact on subjects beyond a questionnaire or observation.
  - Medium risk studies may include the application of substances with no demonstrated toxicity.
  - High risk studies include the application of materials for which there are no toxicology studies, or toxicology studies demonstrate some potential for toxicity.

The IRB Chair, upon notification by the investigator of unanticipated problems involving risk to subjects or others will notify the funding department or agency head in the event of any serious or continuing noncompliance with policies and requirements of the IRB and of any suspension of IRB approval.

- Expedited Review

If an investigator, the IRB Chair, or a qualified designee of the IRB Chair concludes that proposed research is eligible for expedited review per 45 CFR 46.101 (b) and other relevant guidelines (in 45 CFR 46.110, i.e., the research involves no more than minimal risk and falls within the categories published in the November 9, 1998, Federal Register 63 FR 60364-60367; 63 FR 60353-60356 DHHS-FDA list of research eligible for expedited IRB review), that application may be reviewed by the IRB Chairperson or one or more experienced reviewers designated by the Chair, for expedited review. Full review is done if any member recommends referral to the full IRB. In addition, modifications to previously approved research may be eligible

for expedited review. The IRB Chair will report the results of any expedited review to the full IRB at the next scheduled meeting.
In expedited review, the recommendation of the IRB subcommittee (which must be unanimous) will be to:

1. Approve the application as is;
2. Approve it with minor modifications or on condition that certain specified assumptions about the investigator's procedure are correct; or
3. Refer to the full IRB (i.e., the application is not eligible for expedited review).
4. Expedited review cannot disapprove an application or proposed modification. If a reviewer of an expedited application feels that it should be disapproved, he or she should instead refer the proposal to the full IRB for review. If the members of the subcommittee cannot agree on the course of action (as they must make a unanimous decision), the application is automatically referred to the full IRB (i.e., it is not eligible for expedited review).

- Renewals, Reviews, and Completion

The IRB will conduct yearly reviews for all ongoing research, unless more frequent reviews are indicated by degree of risk. Frequency of review is decided by the IRB at the time of approval of the application.

The investigator will notify the IRB Chair whenever a project is completed and provide a summary of the data and results in the termination form and a copy of the final published publication resulting from the research. This information is necessary to maintain IRB files for any possible federal audits.

- Review of Modifications to Previously Approved Research Three types of modifications are distinguished:
    1. Informational modifications that report changes that have no potential implications for human subjects, such as the addition of an associate investigator, a change in title or funding source, a reduction in the number of subjects used, or deletion of items from a questionnaire.
    2. Minor procedural modifications that entail changes in procedures affecting human subjects that do not significantly affect the risks, such as drawing a slightly different amount of blood or adding non-sensitive items to a questionnaire.
    3. Risk-relevant procedural modifications that entail changes in procedures affecting human subjects that significantly affect risks, such as adding a new feature to the treatment of subjects that might increase risk or initiation of videotaping of subjects.

The IRB Chair has the authority to determine into which category a proposed modification falls. Informational and minor procedural modifications may be recorded by the IRB Chair or the Chair's appropriate designee or staff member without review by the full IRB. Risk-relevant procedural modifications are to be referred for subcommittee review if the procedural modification entails minimal risk. The IRB Chair has the authority to determine whether a modification is appropriate for subcommittee review.
Subcommittees will review such modifications using the same procedures as for expedited review as detailed above.

- General Criteria for Institutional Review Board Decisions

The criteria for decisions on human subjects applications are as specified in the federal and international regulations in the area, supplemented by the Sonoran policy as stated in the Student, Faculty, and Clinic Handbooks, in the Research Manual and IRB Principles, Policies and Procedures, and by the applicable laws of the United States and the State of Arizona. When legal advice or assistance is necessary, a request for such assistance will be directed to the President of Sonoran.

If an application involves more than minimal risk to subjects, the IRB must balance risks against their judgment of the scientific merit and importance of the proposed research, hence the likely benefits. Otherwise, the scientific merit of the proposed research is not relevant to the task of the IRB.

In the unusual event of serious concerns about the protection of human subjects that are not clearly covered by any of the references cited herein, the IRB may nevertheless require modifications in the investigator's procedure, or the IRB may defer a decision pending clarification of the relevant regulations, or the IRB may decline to approve the application. In such instances, the IRB Chair will coordinate a meeting of the IRB to clarify and reformulate the Sonoran policy to provide clear criteria for similar instances in the future.

VI Meetings

- Scheduling of meetings

Meetings of the IRB may take place once a month as needed. Some IRB members may meet on an ad how basis as needed according to the expedited review and exemption procedures. Deadlines for receipt of proposal materials is on the first of the month preceding the next scheduled meeting, which will generally be scheduled for the third Friday of the month. Protocol materials are made available online or through e-mail. This schedule permits adequate time for the IRB members to thoroughly review all protocol materials. When a protocol is received, an e-mail invitation to the members of the IRB will be sent detailing:
An agenda for the coming meeting, typically containing:

- a statement on confidentiality of meetings,
- conflict of interest statement(s),
- vote on previous meeting minutes,
- education and information items (including reports to be discussed)
- Recently submitted protocols
- Expedited protocols, changes in protocols,
- Terminations of protocols
- Minutes from the previous meeting.

- Confidentiality

Board meetings are confidential. Proceedings are not to be discussed with non-Board members for any reason. The primary reviewer may seek clarification from the Principal Investigator of a proposal if necessary. Board members may consult in confidence with other Board members about specific issues if necessary. All meeting materials except the agenda and minutes must be returned to the IRB Chairperson each month.

- Conflict of Interest

All Board members must recuse themselves from any discussion regarding a proposal in which they have a conflicting interest, such as co-investigator or consultant, which would compromise the basic IRB principles of fair and impartial review.

- Attendance

a. IRB meetings are scheduled according to the academic calendar and level of need. Meeting times may change each quarter depending on the availability of members. In general, meetings of the IRB will be scheduled for the 3rd Friday afternoon of each month as needed.
b. Members should notify the IRB Chair in the event of unavailability for a monthly meeting. Notification should be given as early as possible so that the Chair is able to assure a quorum at each meeting.
c. Members may be present in person or through audio (telephone) or audiovisual
d. teleconference. Members present via teleconference shall be noted as such in the meeting minutes, which shall also indicate that the members received all pertinent information prior to the meeting and were able to participate actively and equally in all discussions. The standard for members participating by audio or video conferencing is the same for those attending in person, giving all members the opportunity to participate fully in IRB deliberations.

- IRB minutes

IRB minutes shall include documentation of quorum and votes for each IRB action and determination by recording votes as follows:

- Total number voting
- Number for
- Number opposed
- Number abstaining
- Names of those abstaining
- Names of those recusing.

Votes are indicated by voice vote or show of hands.

- Members leaving the meeting room due to a conflicting interest, or for any other reason, will not be recorded as part of the quorum for a particular protocol.
- An individual who is not listed on the official IRB membership roster may not vote with the IRB.
- Ad hoc consultants may not vote with the IRB.
- A non-scientist must always be present for any vote to be taken.

- Review of applications

Introduction

Review of applications by the IRB will specifically include the following regarding safety, fairness and consent:

- Specific aims and purposes of the research
- Procedures to be undertaken to perform the research
- Number and age of subjects
- Inclusion/exclusion criteria
- Subject payment or reimbursement, if any

- Location of research
- Risks to subjects.
- Informed Consent

2. *Safety and confidentiality*

- Risks to subjects are minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk.
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects and the importance of the knowledge that may reasonably be expected to result.
- Selection of subjects is equitable.
- Benefits to subjects and society.
- Financial responsibility for adverse events.
- Confidentiality of data
- Investigational/Non-investigational drug/device toxicity information.
- Informed Consent
  - All eight elements on the checklist are included in the informed consent document
  - Consent form is readable at the 8th grade level
  - Use of jargon and technical terms are minimized
- Letters of participation/cooperation present and appropriate.
- Advertisements/flyers present and appropriate.
- Questionnaires present and appropriate.
- Phone scripts (if necessary) present and appropriate.

A vote of the IRB is taken. The results may be approval, conditional approval if a list of modifications is met, deferral or disapproval. Reasons for conditional approval or disapproval will be listed in the minutes and in the letter to the PI.

A recommendation regarding the risk (low, moderate, high) of the study is assigned.

If necessary, a subcommittee is selected by the chair to follow up on any proposals on which final action cannot be taken.

B. Guidelines for investigators

I. Overview of IRB Process

Any and all research conducted at the college involving human subjects must first be approved by the Research Advisory Board (RAB). The RAB conducts a scientific merit review of all proposals. Upon acceptance by the RAB, the application is then submitted to the Institutional Review Board (IRB), and a human subject safety review is conducted. There is a mandatory application form that must be provided (along with required supporting documents as indicated in the application form) for the IRB to complete this stage of the review. Researchers are urged to consult with the IRB chair prior to submission of any proposal as many questions can be handled ahead of time, reducing the chance of the proposal's rejection.
Once a study is approved, it must be conducted exactly as approved and according to IRB policies. Researchers must submit any proposed changes to the protocol before instituting them. Most proposals are approved for periods of one year. Extension applications can be submitted for longer proposals. Once a study is either terminated or completed, researchers must submit the data, a termination form, a summary of the data, and the published paper that results from the study. This is necessary because the US Food and Drug Administration has the

right to review the IRB files at any time, and evidence of completion or termination of the study is one required element in case such a review were to occur.
The IRB retains the right to audit approved studies at any time without notice to insure compliance.

II. Submission Deadline

All proposal materials are due on the first of each month, without exception, for review at a meeting that occurs approximately on the third Friday of the month.

A cover letter detailing the contents of the submission packet is a necessary document when submitting a packet for IRB review. The purpose is twofold, first to insure the Principal Investigator/study personnel have all the necessary information and second to assist the IRB Coordinator in reviewing the packet.

A copy of current copy of Curriculum Vitae for the Principal Investigator and all investigators must accompany the IRB application. Copies of the OHRP training certificates for all investigators must also be provided.

III. Research involving drugs or investigational devices controlled by the FDA

Research involving drugs and investigational devices as regulated by the FDA 21 CFR 50 and 56

Research at Sonoran must comply with the following FDA regulations for FDA-regulated research involving investigational drugs: 21 CFR §312.7, 21 CFR §312.57, 21 CFR §312.59, 21 CFR §312.60, 21 CFR §312.61, 21 CFR §312.64, 21 CFR §312.66, 21 CFR §312.68, and 21 CFR §312.69.

Research at Sonoran must comply with the following FDA regulations for FDA-regulated research involving investigational devices: 21 CFR §812.7, 21 CFR §812.100, 21 CFR §812.110, 21 CFR §812.145, and 21 CFR §812.150.

And 21 CFR 505(i) and 520(g).

FDA 1572 form

It is also necessary to submit a copy of the FDA 1572 form if the study involves either a drug, device, or biologic regulated by FDA. This statement from the investigator provides assurance that FDA regulations will be complied with.
http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf

IND and IDE

In the event the study is for a new investigational device or drug the IND (Investigational New Drug) or IDE (Investigational Device Exemption) should accompany the protocol and be clearly noted.

Significant Risk and Non-significant Risk Medical Devices Studies

When the protocol uses an investigational device that the investigator considers to be a non-significant risk, the rationale for non-significant risk is included in the protocol application.

IV. Informed Consent Format for Consent Form

The formatted Consent Form explains in easily understood language (8th grade level) the purpose, objectives, and terms of the study. It describes in detail the procedures, laboratory tests, visit schedule, and inclusion/exclusion criteria. The Consent Form must include (45 CFR 46.116)

a. A statement that the study involves research
b. An explanation of the purposes of the research
c. The expected duration of the subject's participation
d. A description of the procedures to be followed
e. Identification of any procedures which are experimental
f. A description of any reasonably foreseeable risks or discomforts to the subject
g. A description of any benefits to the subject or to others which may reasonably be expected from the research
h. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
i. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
j. 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
k. 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
l. 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
m. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant), which are currently unforeseeable
n. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent
o. Any additional costs to the subject that may result from participation in the research
p. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject
q. A statement that significant new findings developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject
r. The approximate number of subjects involved in the study
s. Any additional requirements according to 21 CFR 50.25(b) when investigating material regulated by the FDA

Please follow the format on the sample Consent Form. The IRB may request minor revisions, and it is much easier to make the revisions if the format is followed. If you have a specific

reason to deviate from the format, contact the IRB office, 480-858-9100 Ext. 325 and discuss it with the IRB Chair prior to submission of your packet.

V. Special Requirements - 45 CFR 46 Subpart D - Additional DHHS Protections for Children Involved as Subjects in Research

a. The IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted, or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children, and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances, in which consent may be waived in accord with §46.116 of Subpart A.
b. The IRB may find that the permission of one parent is sufficient for research to be conducted under §46.404 or §46.405.
c. Where research is covered by §46.406 and §46.407, and permission is to be obtained from parents, both parents must give their permission, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
d. If the IRB determines that a research protocol is designed for conditions or for a subject population, for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in Subpart A of this part and paragraph (b) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with Federal, state or local law.
e. Additional Protections for the Inclusion of Children in Clinical Investigations (FDA)

When the protocol involves children as participants, the IRB considers all of the regulations of FDA 21 CFR §50.51, FDA 21 CFR §50.52, FDA 21 CFR§50.53, FDA 21 CFR §50.54, and FDA 21 CFR §50.55 to make the appropriate finding(s) under which the children may be included. Wards: When the protocol involves children who are wards of the state the IRB considers all of the regulations of FDA 21 CFR §50.53, FDA 21 CFR §50.54 and FDA 21 CFR §50.56(a) to make the appropriate finding(s).

IRB Latitude to Approve a Consent Procedure that Alters or Waives some or all of the Elements of Consent 45 CFR 46

§ 46.116 - An IRB may approve a consent procedure, which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent, provided the IRB finds and documents that:
§ 46.116C: 1.The research or demonstration project is to be conducted by, or subject to the approval of, state or local government officials, and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and
§ 46.116C: 2.The research could not practicably be carried out without the waiver or alteration.

§ 46.116D: 1. The research involves no more than minimal risk to the subjects;
§ 46.116D: 2.The waiver or alteration will not adversely affect the rights and welfare of the subjects;
§ 46.116D: 3.The research could not practicably be carried out without the waiver or alteration; and
§ 46.116D: 4.Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

VI. Consent for subjects who do not speak English

Ideally, written consent documents will be written in a form and language that is understandable to the research subjects. Subjects who do no speak English should be presented with a consent document written in a language understandable to them.

Alternatively, (45CFR §46.117B.2) oral presentation of informed consent information in conjunction with a short form written consent document (stating that the elements of consent have been presented orally) and a written summary of what is presented orally may be used. A witness to the oral presentation is required, and the subject must be given copies of the short form document and the summary. The witness must be fluent in both English and the language of the subject.

Legally Required Release of Private Information
The IRB identifies protocols that might collect information that could be subject to a legally mandated release of information, to the extent that this can be ascertained in advance. When such protocols can be identified in advance, the IRB requires that the investigator notify the participant through language in the consent and HIPAA authorization document(s) of the possibility of legally mandated disclosure. Examples of reportable information include:

- Child abuse reporting,
- Elder and dependent adult abuse reporting,
- Sexual assault and rape reporting,
- Warning to police or potential victim when an individual is deemed a danger to others,
- Reporting treatment of person suffering from assaultive or abusive behavior,
- Reporting certain communicable diseases,
- Reporting cases of active TB,
- Reporting disorders characterized by a lapse of consciousness.
- Reporting incidents involving medical devices, 21 USC 360i(b), 21 CFR Part 803.
- Release under a search warrant or a subpoena (e.g., civil or criminal litigation).

VII. Advertisements

If advertisement(s) are planned, it/they must be submitted in their final format with the initial packet. It is often helpful to formulate an advertisement(s) if the possibility exists that the study will eventually have use of them to save time.

VIII. Termination Form

The termination form must be submitted to the IRB when the study is completed.

IX. Disposition of Project Files

All proposed consent forms, outcomes, data, physical exam forms, lab results and final report and manuscript are to be submitted to the IRB Chair.

X. Principal Investigator

Every research project must have a designated single principal investigator who takes personal responsibility for the research. Multiple principal investigators are generally not allowed. The PI must be a full-time faculty member of Sonoran, or one of the designated research adjunct professor, or other individual as agreed upon by the IRB, appointments are required to qualify the PI to receive liability insurance coverage at the College. The PI will also serve as the liaison to the IRB. At the meeting where a research proposal is discussed, the principal investigator must be available. If the investigator is not available, the proposal will be tabled until the next meeting. The principal investigator must maintain all records including the approved protocol, the study's original data, and patient identifying information in a secure manner for seven years after completion of the study. All key personnel listed on the application must submit his/her CV and certificate of completion of the NIH OHRP website training for human subjects research protection.

XI. Investigator conflict of interest

Investigator Conflict of Interest is any situation in which financial or personal interests may compromise or appear to compromise an investigator's professional judgment in conducting or reporting research.

Conflicts of interest may occur when:

- IRB member, investigator, or member of his/her immediate family has or will receive from the sponsor of the research financial or other forms of compensation; or
- IRB member, investigator, or member of his/her immediate family have a significant financial interest in the company/agency/firm that is sponsoring the research; or
- IRB member, investigator or member of his/her immediate family discloses a conflict of interest to the FDA or other agency.

Immediate Family: IRB member or investigator's spouse or domestic partner, minor children, and anyone who resides with the IRB member or investigator or who is the IRB member or investigator's dependent for tax purposes. This will usually be a smaller group of people than the IRB members or investigator's relatives.

Significant Financial Interest: Anything of monetary value, including but not limited to, salary or other payment for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options or other ownership interests); and intellectual property rights (e.g., patents, copyrights and royalties from such rights).

Investigator responsibilities: Investigators are required to disclose Conflicts of Interest on the application for initial IRB review and approval. The investigator must disclose whether he/she or members of his/her immediate family receives financial or other compensation from the study sponsor and/or whether the investigator or members of their immediate families have a significant financial interest in the sponsoring entity. If they answer "yes" to either question, the investigator must (1) provide a description of the relationship between the investigator and/or immediate family with the sponsor of the research, (2) include a statement in the informed consent form that addresses the conflict of interest, or (3) state why such a statement in the informed consent is not necessary for the protection of human subjects.

If an investigator COI develops after IRB approval, the investigator should promptly notify the IRB Administrator and/or IRB chair, submit the change as an amendment (revision) to the approved protocol and include a revised consent form including a statement addressing any potential conflict of interest.

IRB responsibilities: The IRB Administrator will place the application or revision on the upcoming IRB agenda for discussion by the IRB.
The IRB will evaluate whether the conflict of interest will affect the rights and welfare of the subjects participating in the project. Evaluation considerations may include whether disclosure in the consent form is adequate to protect human subjects or if additional safeguards are needed. If the IRB determines that a conflict of interest could affect the rights and welfare of participants, then the conflict of interest must be eliminated or a management plan must be implemented so that the rights and welfare of participants are not affected by the interest.

XII. Adverse Event Reporting

If a research subject in a study approved by the IRB requires medical attention (or in the event of the death of a subject) in the course of the project, the IRB must be notified within 48 hours. The necessary form for such reporting is available from the IRB chair, or on the P drives of the college computer network. Failure to report such adverse events can lead to termination of the research project by the IRB.

XIII. Student Research

Student research is subjected to the same rigorous approval process as any other experiment involving human subjects. Student projects must have a faculty member of the college serve as PI.

Ethical guidelines in communicating research activities with the public.

Informed consent is a critical issue in clinical research. This means that people interested in enrolling in clinical trials are as informed regarding the risks and goals of the research as possible so they can fairly decide whether or not to be a part of the research. This means extreme care must be taken to ensure potential research subjects are given only accurate and honest information, are not mislead in any way, and fully appreciate what will happen to them and why. There must be no coercion, no false promises or misleading hopes, no promises of benefit.

- Advertisements, fliers, brochures prepared to recruit and inform potential participants are part of the informed consent process, and must be approved by the IRB prior to dissemination to the public
- Statements to the public regarding research trials must be truthful and accurate.
- No misleading statements, including over-interpretation of hoped-for results
- In other words, don’t say what the results of the study will be
- No statements such as “we will demonstrate the benefit of this treatment for this condition,”
- It is permissible to state the study is investigating the effects of a substance on a given group of subjects
- No promises to the potential participant
- No bribes or unreasonable incentives
- $20 for time may be reasonable

Reports to the IRB must be made within 48 hours of:

- An unanticipated problems involving risks to subjects or others
- Serious or continuing non-compliance with federal or institutional requirements
- Suspension of any research activities due to non-compliance

XIV. All personnel involved in clinical research at Southwest College must provide a certificate of completion from Protecting Human Research Participants at http://phrp.nihtraining.com/users/login.php).

a. Internet site for references and further training
   i. NIH Bioethics Resources by NIH http://www.nih.gov/sigs/bioethics/index.html
   ii. FDA Guideline for IRB and Investigators http://www.fda.gov/oc/oha/IRB/toc.html
   iii. AAMC Research Compliance Resource
   iv. https://www.aamc.org/advocacy/research/clinical/humansubj/
   v. CDC Human Subjects Research http://www.cdc.gov/od/science/integrity/hrpo/
   vi. Office for Human Research Protections http://www.hhs.gov/ohrp/
   vii. Office of Human Subjects Research http://ohsr.od.nih.gov/

XV. Required Product Information

1. Quality assurance/quality control from the manufacturer
   a. Manufacturer information: name, address
   b. Manufacturing procedure: process following cGMP, GLP, and DSHEA recommendations
   c. Certificate of analysis, quality assurance, quality control, and consistency of product
   d. Confirmation that study products will be from single, identifiable batch
2. IND, NDA, GRAS status, notification letters, other status with the FDA, or other government agencies if applicable. Submit copies of all documents.
3. Ingredient information
   a. Detailed ingredient list and specific amounts and dosages: active and inactive
   b. Detail information on each ingredient, literature reviews, monographs, references, etc.
4. Toxicology and/or pharmacology profile
   a. Review of literature
5. Pharmacodynamics, pharmacokinetics, and bioavailability
   a. Mechanism of action
   b. Potential/hypothesis of mechanism of action
6. Protocol: dose frequency, length of treatment, timeline, special instructions
7. Current outcomes data/field report and/or anticipated outcomes
   a. Anticipated objective outcomes
   i. Clinical effects
   b. Anticipated subjective outcomes
   i. Physical
   ii. Biochemical, physiological, structural, etc.
   c. Physical, emotional, mental, behavioral, etc. if applicable
8. Adverse events, risks, drug interactions, toxicity, precautions, contraindications, special instructions. Include findings from:
   a. Field reports
   b. Published reports: preclinical (animal), in vitro, in vivo, clinical studies
   b. Adverse events anticipated
   c. Adverse events in theory

9. Intervention products
    a. Final product samples must be sent to PI prior to distribution of any products
    b. Extra products must be provided for each study group (5-10% of study products)
    b. Individual codes sealed in envelopes per study subject plus one master code must be provided
    c. Product label should include code, batch number, expiration date, and dose instructions and emergency call #.

XVI. Sonoran Research Insurance Coverage Protocol

Research projects conducted by Sonoran, if funded by a corporate sponsor, outside foundation or organization, will need to have project specific liability insurance coverage from the current Sonoran insurance policy. Internally funded projects will not need this project specific liability insurance coverage.

Full-time and part-time faculty are covered by our general liability and researcher liability as long as he/she is on our biweekly payroll AND working on Sonoran business.

The need for project specific liability insurance and the level of project risk will be determined by the project principal investigator(s) and dean. The cost of additional insurance coverage will be determined by our insurance company based on the risk rate and research plan summary. For current rates for insurance coverage see the CFO.

The following project information must be submitted to the Sonoran CFO for insurance coverage if funded by a corporate sponsor, outside foundation or organization. Approval of insurance coverage will be required prior to start of project. The CFO will communicate with the insurance company to secure the insurance coverage and rate. Internally funded projects will not need insurance coverage or submission of project information to the Sonoran CFO.

- PI:
- Project title:
- Sample population:
- Condition being studied:
- Number of patients:
- Treatment/intervention period:
- Treatment/intervention protocol:
- Risk rate:
- Study start date:

The information should be no more than 1 to 2 sentences per item. Below is a sample research plan summary.

- PI: Must be full-time faculty at Sonoran or Research Associate at SCRI
- Project title: Efficacy of antioxidants in reducing high cholesterol. A randomized controlled clinical trial.
- Sample population: 45 to 64 yo men and women
- Condition being studied: Elevated lipid profile
- Number of patients: 50.
- Treatment period: 30 days
- Intervention protocol: Combination antioxidants supplements taken orally once a day

- Risk rate: Low
- Study start date: 5/1/2000

Research project risk rate is defined as the following (Assigned by the IRB):

- No Risk = No intervention protocol and no risk of adverse events for the participants
- Low Risk = Intervention protocol with low risk of adverse events for the participants
- Moderate Risk = Intervention protocol with moderate risk of adverse events for the participants
- High Risk = Intervention protocol with high risk of adverse events for the participants

Liability Insurance Coverage

The PI, investigators and student research assistants will be covered as long as they are strictly working on behalf of Sonoran. The faculty investigators must be a full-time employee or on payroll at Sonoran to receive the coverage. Other research investigators listed on the project will not be covered unless specified.

Research projects conducted at the college, clinic or at an approved off site facility that Sonoran has a contract with for the project will be covered. Non-Sonoran employees collaborating on the project will not be covered by the Sonoran liability insurance. The collaborators wanting coverage by Sonoran liability insurance coverage for the project must have proof of insurance showing general liability, workers compensation and medical malpractice. The collaborators must also name Sonoran as an additional insured.

Student Research Participation

- Sonoran students can participate in clinical research by assisting investigators in all aspects of the research project. The extent of research assistance by students will vary based on active preceptorship filed with the Arizona State Naturopathic Physicians Board of Medical Examiners.
- Sonoran Students not at clinic (patientcare)
- Students are allowed to perform the following research assistance: subject screening, interviewing, scheduling, phone call monitoring, data collection, data entry, clinical coordination, distributing and collecting informed consent and study questionnaires/forms, collecting vitals (weight, height, temperature, radial pulse, respiration rate, and blood pressure), and distributing study intervention.
- Students are not allowed to perform any patient procedures, physical examination (except vitals), phlebotomy, sign the informed consent, or provide treatment, diagnosis, or medical advice.
- Students are not eligible to receive clinical training credit for patient contacts for the research project.
- Students will be supervised by a licensed clinical investigator (supervising physician) at all times during patient assistance at the medical center. Supervision means to be physically present within sight or sound of a medical student who is providing assistance with the research project. The supervising physician must be at the medical center during student assistance with research patient contacts.

Sonoran Students at clinic (patientcare)

- Students are allowed to perform the following research assistance: subject screening, interviewing, scheduling, phone call monitoring, data collection, data entry, clinical coordination, distributing and collecting informed consent and study questionnaires/forms, collecting vitals (weight, height, temperature, radial pulse, respiration rate, and blood pressure), and distributing study intervention.
- Students are allowed to perform limited patient procedures including physical examination, phlebotomy, and sign the informed consent.
- Students are not allowed to provide treatment, diagnosis, or medical advice.
- Students are eligible to receive clinical training credit for patient contacts for the research project.
- Students will be supervised by a licensed clinical investigator (supervising physician) at all times during patient assistance at the medical center. Supervision means to be physically present within sight or sound of a medical student who is providing assistance with the research project. The supervising physician must be at the medical center during student assistance with research patient contacts.

Student Research Projects
Student research projects at Sonoran is required to have a PI who is a Sonoran full-time faculty, and thus will follow the same policies and procedures as described above.

C. Fee Schedule

A fee will be assessed all applications to the IRB to offset expenses. These fees may be waived unless:

- The research is supported by a federal grant
- The research is supported by industry grants or contracts
- The research is originated from outside the college. Charges will be

IRB review, full initial review $500 IRB review, full continuing review $300 IRB review, expedited initial review $300 IRB review, expedited continuing review $200

Protocols withdrawn after review and then resubmitted will be charged as new protocols.
No charge for review of amendments/modifications that do not require full IRB review. No charge for adverse events reports, protocol deviation/violation reports, or emergency requests. Recruitment materials submitted after initial or continuing review may be subject to an additional charge.

D. Sonoran Research Organizational Chart