Overview of Basic IRB Regulations

I. Federal Regulations
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II. IRB Authority and Composition

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Federal Policy
For the Protection
of Human Subjects

* Effective 1991

* Adopted By 18 Federal Agencies

* Based on Subpart A 45 CFR 46

Department of Health & Human Services
Protection of Human Subjects
45 Code of Federal Regulations Part 46

* Core Requirements Subpart A
  August 1991

* Pregnant Women, Human Fetuses, and Neonates
  Subpart B
  Revised November 2001

* Prisoners Subpart C
  November 1978
  [OHRP Guidance May 2003]

* Children Subpart D
  March 1983
Research Category 1: Not Greater than Minimal Risk

(46.404 and 50.51)

The IRB must find that:

1. Adequate provisions have been made for soliciting the assent of the children as set forth in 46.408 and 50.55;

2. Adequate provisions have been made for soliciting the permission of their parents or guardians as set forth in 46.408 and 50.55; (Permission of one parent is sufficient, if approved by the IRB.)

Research Category 2: Greater than Minimal Risk, but Prospect of Direct Benefit to Individual Subjects (46.405 and 50.52)

IRB must find that:

1. Risk is justified by anticipated benefit;

2. Relation of the benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches;

3. Adequate provisions are made for soliciting assent of children and permission of their parents or guardians; (Permission of one parent is sufficient, if approved by the IRB.)
**Research Category 3**: Greater than Minimal Risk, No Prospect of Direct Benefit to Individual Subjects, but Likely to Yield Generalizable Knowledge about the Subject's Disorder or Condition (46.406 and 50.53)

IRB must find that:

1. Risk represents a minor increase over minimal risk;

2. The intervention or procedure presents experiences to the subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations;

3. The procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for understanding or amelioration of the subjects' disorder;

4. Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians; (except under specific circumstances, permission must be obtained from both parents).

**Research Category 4**: Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (46.407 and 50.54). To approve requires:

1. IRB finds the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem.

2. Review by the HHS Secretary and FDA Commission after consultation with a panel of experts and public comment.
Applicability: HHS

* Submitted To HHS
* Conducted / Funded By HHS
* Involves Research
* Involves Human Subjects

Definition of “Research”

"A Systematic Investigation Designed To Develop or Contribute To Generalizable Knowledge" [45 CFR 46.102 (d)]

Definition of "Human Subject"

“A Living Individual About Whom an Investigator... Conducting Research Obtains (1) Data Through Intervention or Interaction With the Individual, or (2) Identifiable Private Information.” [45 CFR 46.102(f)]
Exemption Categories

Research activities are exempt from the Federal Policy for the Protection of Human Subjects when the ONLY involvement of human subjects falls within one or more of the categories below.

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices.

2. Research involving the use of educational tests, survey procedures, interview procedures or observation of public behavior, unless: (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; AND (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation. For Veteran Affairs Medical Center (VAMC) research, damage to the subjects' insurability must also be taken into consideration.

3. Research not exempt under "2" above may be exempt if: (i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter (e.g., Department of Justice and National Center for Educational Statistics).
4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

PLEASE NOTE: According to the Office for Human Research Protections (OHRP), “to qualify for this exemption the data, documents, records, or specimens must be in existence before the project begins.”

5. Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are 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; (v) projects for which there is no statutory requirement for IRB review; (vi) projects that do not involve significant physical invasions or intrusions upon the privacy interests of participants; (vii) authorization or concurrence by funding agencies that exemption from IRB review is acceptable.

6. Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome food without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.
For Institutions with HHS Approved Assurances

All Exemption Categories Do Not Apply To Research Involving:

* Prisoners

Exemption Category #2 - Survey/Interview

* Does Not Apply To Research Involving Children

Exemption Category #2 - Observation Of Public Behavior

* Does Not Apply to Research which Involves the Observation of Minors where the Investigator Participates in the Activities Being Observed

Exemption Categories #1-5

* Does Not Apply to FDA-regulated Research
HHS Federal Wide Assurance*

* Revised Procedures Effective December, 2000

* Requires IRB Registration

* Requires Only One Type of Assurance

* Includes Web Course for IRB Chair, Staff & Designated Institutional Official

* Includes Recommendations for Investigator, Research Staff, & IRB Member Education

* http://www.hhs.gov/ohrp/assurances/index.html

[NOTE: FDA Does Require Written Procedures But Does Not Require Approved Assurance]
IRBs Must Have Written Procedures For:

1. Conducting initial and continuing review and reporting findings and actions to investigator and institution.

2. Determining which projects require review more often than annually.

3. Determining which projects need verification from sources other than investigator that no material changes have occurred since previous IRB review.

4. Insuring prompt reporting to IRB of proposed changes.

5. Insuring that changes may not be initiated without IRB review and approval.

6. Insuring prompt reporting to IRB, institution, and agency of unanticipated problems, serious or continuing noncompliance, and suspension or termination of IRB approval.
Office for Human Research Protection

The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, MD  20852
(240) 453-6900

OHRP Policy and Guidance

http://www.hhs.gov/ohrp/policy/index.html

NIH Policy

“Guidelines for the Inclusion of Women and Minority as Subjects in Clinical Research”

*Effective March, 1994

"Guidelines for the Inclusion of Children in Research Involving Human Subjects"

*Effective October 1, 1998

“Required Education in the Protection of Human Research Participants”

*Effective October, 2000
**Food and Drug Administration**

*Informed Consent 21 CFR 50*

*Subpart D Children*

*Institutional Review Board 21 CFR 56*

**Applicability: FDA**

* Clinical Investigations

* Regulated Products, Drugs
  Devices, Biologics, Food/Color
  Additives

**"Clinical Investigation" Definition**

* Involves use of a Test Article

* One or more Human Subjects

* Meets Requirements for Prior Submission to FDA, or

* Results Intended to be Part of an Application for Research or Marketing Permit [21 CFR 56. 102 (c)]
Food and Drug Administration Definition

"Emergency Use"

* Use of a Test Article on a Human Subject
  In a Life Threatening Situation

* In Which No Standard Acceptable
  Treatment is Available

* In Which There is Not Sufficient Time To
  Obtain IRB Approval [21 CFR 56.102 (d)]

"Emergency Use" of a Test Article is
Exempt from IRB Review:

* Provided "Emergency Use" is Reported to IRB
  Within 5 Working Days

* Any Subsequent Use of the Test Article at the
  Institution is Subject to IRB Review
  [21 CFR 56.104 (c)]
Related FDA Regulations

**Investigational Drug Exemption**

21 CFR 312, 314

Investigation New Drug, Antibiotic & Biological Drug Product Regulations

FDA 21 CFR Part 312

* Subpart A 312.2(b) Applicability Exemptions

* Subpart B 312.34 Treatment Use

* Subpart A 312.7 Sale of Investigational Drugs

**FDA Medical Devices**

* 21 CFR 812 Investigational Device Exemptions

* 21 CFR 814

**FDA Office for Good Clinical Practice**

Food and Drug Administration
5600 Fishers Lane, HF-34
Parklawn Building, Room 9C-24
Rockville MD 20857
Telephone: 301-827-3340
Facsimile: 301-827-1169

Email: gcpquestions@oc.fda.gov
**Veterans Affairs**

* 38 CFR Part 16

* VA Administration Handbook

* Office of Research Oversight (ORO)
  (202) 565-4835

* Program for Research Integrity Development & Education (PRIDE)
  (202) 254-0282

* NCQA VA Human Research Protection Accreditation Program

**Additional Requirements**

* International Conference on Harmonisation/Good Clinical Practices

* Joint Commission on Accreditation of Healthcare Organizations

* U.S. Department of Education
  - Subpart in Children
  - Additional Membership Requirements
  - No Child left Behind

* Association for the Accreditation of Human Research Protection Programs & Partnerships for Human Research Protection

* Confidentiality Certificates DHHS


* Health Insurance Portability and Accountability Act of 1996 (HIPAA)
Authority of IRB

* Approve, Disprove or Modify
* Conduct Continuing Review
* Observe/Verify Changes
* Suspend or Terminate Approval

IRB Membership

* At Least Five Members
* Both Genders, if Possible
* Varied Professions
* Member Whose Primary Concerns are in Nonscientific Areas
* Member Whose Primary Concerns are in Scientific Areas
* Member Not Otherwise Affiliated with the Institution
IRB Membership

* Experience and Expertise

* Diversity of Backgrounds

* Sensitivity to Community Attitudes

* Knowledge of Institutional Commitments and Regulations, Applicable Law, Standards of Professional Conduct

* Knowledgeable and Experienced with Vulnerable Subjects

* Special Competencies of Ad Hoc Consultants

Mechanisms for Review

* Expedited Review

* Full Review
Requirements for Conducting An Expedited Review

1. IRB may use an expedited review procedure if the following conditions exist:
   a. research involves no more than minimal risk and;
   b. the only involvement of human subjects is in one or more federally specified categories.

2. Expedited procedures can also be used to review minor changes in previously approved research.

3. Review can be conducted by chairperson.

4. The review can be conducted by one or more reviewers designated by the chairperson from among members of the IRB. (Note that members with conflict of interest cannot serve as an expedited reviewer.)

5. The reviewer may exercise all of the authorities of the IRB except the reviewer may not disapprove research.

6. In conducting the review, a determination must be made that the research meets the conditions required for use of expedited procedures.

7. To approve the research, the reviewer must make the determination that all of the requirements specified in 45 CFR 46.111 and 21 CFR 56.111 are satisfied.

8. The IRB must adopt a method for keeping all members advised of research proposals which have been approved using expedited procedures.
Criteria for Conducting Expedited Review

* No More Than "Minimal Risk" And
* Falls in One or More Federally Specified Categories
  - Categories apply regardless of age
  - Categories do not apply if identification places subjects at risk or damage or stigmatization
  - Do not apply to classified research
  - Standard informed consent requirements do apply

* Minor Change in Previously Approved Research

"Minimal Risk"

"The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests."
[45 CFR Part 46 102(f) and 21 CFR Part 56.102 (i)]
Research Categories For Conducting Expedited Review
Effective November 9, 1998

Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
   
a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for Expedited review.)

b. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
   
a. From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

b. From other adults and children\(^1\) considering the age, weight, and health of the subjects, the collection
procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means.
   Examples: (a) Hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding 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.)
Examples: (a) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects 45 CFR 46.101 (b)(2) and (b)(3). This listing refers only to research that is not exempt.)
8. Continuing review of research previously approved by the convened IRB as follows:

   a. Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
   b. Where no subjects have been enrolled and no additional risks have been identified; or
   c. Where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

1 Children are defined in the HHS regulations as “persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.” [45 CFR 46.402(a)]
Requirements for Conducting
A Full Review

1. Review must be conducted at a convened meeting.

2. A majority of the members of the IRB must be present at the meeting.

3. 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.)

4. To approve research, the IRB must determine that all of the requirements specified in 45 CFR 46.111 are satisfied.

5. For research to be approved, it must receive approval of a majority of the members present at the meeting.

6. IRB members who have a conflicting interest in a research project cannot participate in the review except to provide information requested by the IRB, and then must be absent themselves for the final discussion and vote.

7. The IRB must notify investigators and the institution in writing of its decision to approve, modify or disapprove the research.
Types of Review

* Initial Review
* Continuation Review
* Amendment Review
* Adverse Reaction
* Noncompliance

Requirements for Conducting Continuation Review

1. Continuing review of research must be conducted at intervals appropriate to the degree of risk, but not less than once per year (i.e., IRB cannot approve a research project for more than 12 months).

2. When conducting a continuation review, "Full Review" procedures should be used unless the research meets the expedited review criteria.

3. To approve research, the IRB must determine that all the requirements specified in 45 CFR 46.111 and 21 CFR 56.111 are satisfied.

4. In full review, all IRB members should review protocol summary/status report that includes:
   - The number of subjects accrued;
   - A summary of adverse events and any unanticipated problems involving risks to subjects or others, any withdrawal of subjects from the research, or complaints about the research since the last IRB review;
   - A summary of any relevant recent literature, interim findings,
and amendments or modifications to the research since the last review;
• Any relevant multi-center trial reports;
• Any other relevant information, especially information about risks associated with the research; and
• A copy of the current informed consent document and any newly proposed consent document.

[July 2002 OHRP Guidance]

5. At least one member should review complete protocol.

6. Minutes of IRB meeting should document separate deliberations and votes for each continuing protocol review at convened meeting.
Ethical Principles

* Respect for Persons
  Consent, Privacy, Confidentiality

* Beneficence
  Benefit vs. Risk

* Justice
  Equitable Selection

[Belmont Report, 1979]

Main Function of IRB Review
To Assure That:

* Risks are Minimized by Using Procedures that are Consistent with Sound Research Design and Which Do Not Unnecessarily Expose Subjects to Risk, and Whenever Appropriate, by Using Procedures Already Being Performed on the Subjects for Diagnostic or Treatment Purposes;

* Risks to Subjects are Reasonable in Relation to Anticipated Benefits

* There is Informed Consent

* Rights and Welfare of Subjects are Maintained
To approve research, an IRB should determine that all of the following conditions exist:

1. Risks to subjects are minimized by using procedures that are consistent with sound research design and which do not unnecessarily expose subjects to risk, and whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects and importance of the knowledge that may reasonably be expected to result.

3. Selection of subjects is equitable.

4. Informed consent will be sought.

5. Informed consent will be documented.

6. Where appropriate, the research plan makes adequate provision for monitoring the data collected to insure safety of subjects. (At UK, this applies to greater than minimal risk studies, clinical research, or a NIH funded/FDA regulated clinical trial)

7. There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

8. Where any of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect subjects.
**Informed Consent**

* 5 Sets of Requirements*

* General Requirements

* Basic Elements

* Additional Elements

* Alteration or Waiver

* Documentation
General Requirements for Informed Consent
45 CFR Part 46.116

Legally effective informed consent shall:

1. be obtained from the subject or the subject's legally authorized representative;

2. be in language understandable to subject or representative;

3. be obtained under circumstances that provide subject with opportunity to consider whether or not to participate, and that minimize coercion influences;

4. not include language through which subject is made to waive any of his legal rights or which releases the investigator, sponsor or institution from liability for negligence.
Basic Elements of Informed Consent
45 CFR Part 46.116(a)
21 CFR Part 50.25(a)

1. Statement that study involves research; explanation of purposes of research and expected duration of subject's participation; description of procedures to be followed and identification of any procedures which are experimental.

2. Description of risks or discomforts to subject.

3. Description of benefits to subject or to others.

4. Disclosure of alternative procedures, if appropriate.

5. Description of the extent to which confidentiality will be maintained.

   FDA: statement that FDA may inspect records.

6. For research involving more than minimal risk, explanation as to whether compensation and medical treatments are available if injury occurs.

7. Explanation of whom to contact if questions arise about: a) the research; b) the subjects' rights; or c) whom to contact if research-related injury occurs.

8. Statement that participation is voluntary, that refusal to participate involves no penalty or loss of benefits, and that subject may discontinue at any time.
Additional Elements of Informed Consent
45 CFR Part 46.116(b)
21 CFR Part 50.25 (b)

When required by the IRB, one or more of the following elements shall be provided to each subject:

1. Statement that procedure may involve unforeseeable risks;
2. Description of circumstances under which subject's participation may be terminated by the investigator without subject's consent;
3. Additional costs to subject resulting from participation in research;
4. Consequences of subject's decision to withdraw from research;
5. Statement that significant new findings developed during research which may relate to subject's willingness to continue will be provided to subject;
6. Approximate number of subjects involved in study.
HHS Exceptions From Requirement
For Informed Consent*
45 CFR 46.116(c) (d)

1. An IRB may waive requirement or alter element if it finds and documents that:

   a. research involves no more than "minimal risk";

   b. rights and welfare of subjects will not be adversely affected;

   c. research could not practicably be carried out without waiver or alteration;

   d. when appropriate, the subjects will be provided pertinent information after participation.

2. An IRB may waive the requirement to obtain informed consent or alter some of the elements if the IRB finds and documents that:

   a. the research or demonstration project is to be conducted by or subject to approval of state or local government officials and is designed to study, evaluate or examine public benefit of service programs or proposed changes in programs, procedures, methods or levels of payment AND

   b. the research could not practicably be carried out without the waiver or alteration.

*[NOTE these criteria are not included in the FDA regulations. Both HHS and FDA have additional requirements for waiving informed consent in research involving emergency or acute care.]
FDA Exceptions From Requirements
For Informed Consent*
[Singale Patient Administration]
21 CFR 50.23

1. Obtaining informed consent may be waived if both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:
   a. Subject is in life-threatening situation necessitating use of test article;
   b. Consent cannot be obtained because of an inability to communicate with or obtain consent from the subject;
   c. Time is not sufficient to obtain consent from subject's legal representative;
   d. No alternative generally approved method is available.

2. If immediate use of the test article is required to save the life of the subject and time is not sufficient to obtain independent determination by another physician, a determination by the investigator shall be made.

3. This determination is to be reviewed and evaluated in writing by a physician who is not participating in the investigation within 5 days after use of article.

4. The documentation required in 1, 2 or 3 above must be submitted to the IRB within 5 working days after use of test article.

[*Note these requirements are not included in HHS regulations. FDA and HHS have additional requirements for waiving informed consent in research projects involving emergency or acute care. FDA 21 Part 50.24, DHHS 45 CFR Part 46.101(i)]
Research Projects Involving Emergency or Acute Care

To Approve Acute Care Informed Consent Waiver, Institutional Review Board (IRB)\(^1\) must find and document FDA 21 Part 50.24, DHHS 45 CFR Part 46.101(i)\(^2\):

1. Administration involves life threatening situation; Available treatment unproven or unsatisfactory; Collecting of evidence necessary to determine safety and effectiveness

2. Obtaining consent NOT feasible because:
   a. Subject’s medical condition
   b. Intervention must be administered before feasible to consent legally authorized representatives
   c. No reasonable way to identify prospective subjects

3. Research of potential direct benefit to subjects:
   a. Life threatening situation necessitates intervention
   b. Animal and preclinical studies support potential direct benefit of intervention for individuals
   c. Risks reasonable in relationship to
      1. What is known about medical condition
      2. Risks and benefits of standard therapy
      3. Risks and benefits of proposed intervention

4. Investigation could NOT practicably be carried out without waiver
5. Investigator has:
   a. Defined length of potential therapeutic window
   b. Is committed to attempting to contact and obtain consent from legally authorized representative within window
   c. Will summarize efforts to contact authorized representative at the time of continuing review
   d. Is committed to contact within window subject’s family member\(^3\) and ask if he/she objects (if obtaining consent from subject or legally authorized representative is not feasible)
   e. Will summarize efforts to contact family member at the time of IRB continuing review

6. IRB has:
   a. Approved informed consent procedures and documents to be used with subject/legally authorized representative
   b. Approved procedures and information to be used when providing family members opportunity to object

7. Consultation with representatives of communities from which subjects will be drawn and in which research will be conducted

8. Public disclosure in communities prior to initiation including:
   a. Plans for study
   b. Risks and benefits
9. Public disclosure to community at completion of study including:
   a. Demographics of population
   b. Results of study

10. Establishment of an independent data and safety monitoring committee

11. Procedures are in place to inform at earliest opportunity each subject (if competent), legally authorized representative, and/or family member of:
   a. Subject’s inclusion in study
   b. Details of study and other information in informed consent document
   c. Opportunity to discontinue subject’s participation without penalty or loss of benefit to which subject is entitled

12. Additional reporting and recordkeeping, FDA drug and device application requirements must be met [These are outlined in attached document]

Footnotes

- IRB review must include concurrence of a licensed physician who is a member or a consultant to IRB and who is not otherwise participating in the clinical investigation.
- For Department of Health and Human Services (DHHS) regulated studies, waiver not applicable to research involving prisoners, fetuses, pregnant women, human in vitro, and fertilization.
- “Family member” is defined as any one of the following legally competent persons: spouse, parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.
1. For Food and Drug Administration (FDA) regulated investigations, a separate Investigational New Drug application (IND) or Investigational Device Exemption (IDE) is required
   a. Separate IND/IDE identifies protocol as including subjects unable to give consent
   b. Submission of separate IND/IDE required even if IND/IDE for same drug/device exists
   c. Applications may not be submitted to FDA as amendments

2. If research is NOT subject to FDA 21 CFR Part 50, but DOES fall in purview of DHHS 45 CFR Part 46, the IRB must report to the Office for Human Research Protections (OHRP) that approved acute care informed consent waiver has occurred. [Note: The conditions for approval of DHHS are identical to those outlined in FDA 50.24]

3. If the IRB does NOT approve request for waiver:
   a. IRB must document findings including reasons for disapproval and promptly provide to:
      1. clinical investigator
      2. sponsor
b. Sponsor must promptly report disapproval to:

1. FDA
2. Other clinical investigators in this or substantially equivalent clinical investigations
3. Other IRBs reviewing this or substantially equivalent investigations

4. If waiver is approved:
   
a. IRB must provide sponsor with copy of information that has been publicly disclosed prior to initiation and at completion of study [Investigator must provide IRB with information]

   b. Sponsors must provide copies to FDA

5. IRB, Investigator, and Sponsor records must be:

   a. retained for three years after completion of clinical investigation

   b. accessible for inspection and copying by FDA
Documentation of Informed Consent

45 CFR Part 46.117(a)(b)
21 CFR Part 50.27

1. Informed consent will be documented using:
   a. a written form approved by the IRB
   b. a written form the subject or legally authorized representative has had opportunity to read before signing
   c. a written form signed by the subject or his legal representative. [For FDA the subject also dates form]

2. A copy must be given to the person signing the form.

3. Two types of consent forms are permissible:
   a. written consent document that includes all of the basic elements of informed consent;
   b. short form which states that the elements of informed consent have been presented orally to the subject. When using the short form the following conditions must be met:
      1. the written summary of what is to be said receives prior approval of the IRB;
      2. a witness must be present at the oral presentation;
      3. the short form is signed by the subject or his legal representative [For FDA the subject also dates form];
      4. the witness signs both the short form and a copy of the written oral presentation;
      5. person obtaining consent shall sign a copy of the summary;
      6. a copy of both the short form and the written summary is given to the person signing the form.
Exceptions to Documenting Informed Consent
45 CFR 46.117(c)

1. IRB may waive requirement to obtain a signed consent form for some or all of subjects if:
   a. the only record linking the subject and the research would be the consent document and the principal risk would be harm resulting from breach of confidentiality; each subject must be asked whether subject wants documentation; or
   b. the research presents no more than minimal risk and involves no procedures for which written consent is normally required.

2. In cases where documentation is waived, the IRB may require investigator to provide subjects with written statement regarding the research.

[Note that 1a above is not included in FDA. 1b is included in FDA and HHS regulations 21 CFR 56.109(c)]
**Reporting Requirements**  
**To IRB, Institution, Agency**

* Unanticipated Problems

* Serious or Continuing Noncompliance

* Suspension or Termination

**Additional Reporting Requirements**

* IRB Actions to PI and Institution

* IRB Membership Change to OHRP

* Requirements Specific to Selected Regulations
IRB Records
45 CFR Part 46.115
21 CFR Part 56.115

* Research Protocols/Consent Documents
  [Examples: Grant Applications, Physicians Brochure, Sponsor Protocol, IRB Application]

* Correspondence Between IRB and Investigator

* Continuing Review
  [Examples: Progress Report, Amendments, Adverse Effect, Noncompliance]

* Meeting Minutes
  [Attendance, IRB Action, Vote & Number, Basis of Decisions, Summary of Controverted Issues, Discussion of Federally Required Special Findings]

* Membership
  [Name, Degrees, Representative Capacity, Experience, Relationship to Institution]

* Written Procedures
  [As specified in 45 CFR 46.103(b)(4)(5) & 21 CFR 56.108(a)(b) in VA and OHRP Guidance on Standard Operating Procedures]

* Significant New Findings

* Maintain Records Three Years After Completion of Project*

* State Law, Regulatory Funding Agency or Local Policy may Require Longer Retention Period

* HIPAA: Six Year Requirement