AGENDA:
- Overview of the Tulane University HRPP
- Guidance on Protecting Human Subjects in Research
  (Preparation for AAHRPP Re-Accreditation Site Visit)
  AAHRPP Site Visit (MAY 29, 2013 - MAY 31, 2013)

OVERVIEW OF TULANE HRPP
- What is an HRPP?
  A Human Research Protections Program is an integrated
  process where all the various components of an
  organization involved in the conduct of human research
  work together to protect the rights and welfare of
  participants.
- HRPP \rightarrow Not an office
- HRPP \rightarrow A collective effort of all who participate in the
  conduct, review, approval, and facilitation of human
  subjects research at Tulane University
**AAHRPP/RE-ACCREDITATION**

- AAHRPP's Mission: The Association for the Accreditation of Human Research Protection Programs, Inc (AAHRPP) accredits high-quality human research protection programs in order to promote excellent, ethically sound research. [http://www.aahrpp.org/](http://www.aahrpp.org/)
- Tulane University achieved accreditation for its Human Research Protection Program (HRPP) on September 17, 2010 and is in the process of undergoing Re-Accreditation from AAHRPP.
- The AAHRPP site review team will once again be on campus to conduct a site visit and will interview members of the HRPP.

**SITE VISIT MAY 29, 2013 - MAY 31, 2013**

**EDUCATION**

- Human Subjects Research Education:
  All individuals involved in human subjects research at Tulane University must complete the CITI course.
  Group 1 - Biomedical Researchers & Key Personnel
  Group 2 - Social/Behavioral Researchers & Key Personnel
- Tulane requires CITI re-certification every 4 years.
- Other Education:
  GCP Education
  HRPO Education
  Research Staff Education
RESOURCES

- What resources are you provided regarding the protection of human research subjects?

- To whom do you go for help on issues, such as regulatory or ethical?

  - The HRPO; irbmain@tulane.edu
  - Federal Regulations
  - Colleagues
  - The IRB (Chair, Members, Staff)

THE IRB

- What does the Institutional Review Board (IRB) do?

- There are 2 IRBs at Tulane University:
  - Biomedical IRB
  - Social/Behavioral IRB

- The IRB reviews and approves research in accordance with the DHHS Regulations (for all human subjects research), FDA Regulations (for studies involving products regulated by the FDA), and complies with HIPAA Regulations.

  http://www.hhs.gov/ohrp/
  http://www.fda.gov/
  http://www.hhs.gov/ocr/privacy/hipaa/administrative/privacyrule/
RISK

- Minimal Risk:
  According to the Federal Regulations, "minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater than in and of themselves than those ordinarily encountered in daily life or during the performance of a routine physical or psychological examinations or tests."

- This definition serves as the starting point for the IRB's determination of the category of review.
  
  Minimal Risk → Exempt or Expedited Review
  > Minimal Risk → Full IRB Review at a Convened IRB Meeting

- The IRB is to determine if the risks to subjects have been minimized appropriately and if the risks are reasonable in relation to the expected benefits of the research.

PRIVACY & CONFIDENTIALITY

- An issue of primary importance in the protection of human subjects in research is the protection of privacy and confidentiality.

- Privacy can be defined in terms of having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.

- Confidentiality pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others in ways that are inconsistent with the understanding of the original disclosure without permission.
PRIVACY & CONFIDENTIALITY

- The IRB must decide on a case-by-case (e.g., study by study) basis whether there are adequate provisions to protect the privacy of the subjects and to maintain the confidentiality of the data.

- The IRB considers the following:
  - Efforts to code or de-identify data
  - How the informed consent process will take place
  - The storage of records/files
  - Appropriate safeguards for long term retention of records
  - Special protections for video/audio taped data and photographs of subjects

CONSENT

- Obtaining Consent is a basic ethical obligation for researchers.

- While the informed consent process is prospective and takes place prior to any research activity, consent should also be an ongoing educational interaction between the investigator, the research staff, and the research subject that continues throughout the study.

- Minors and those individuals who are not competent to provide consent should be given the opportunity to Assent to participate in the research project. The IRB recommends that children ages 7 and older be given the opportunity to assent.
WAIVERS OF CONSENT

• Waiving the Documentation of Consent:

  • In some situations, the IRB may waive the requirement for obtaining a signed Informed Consent Document. The regulations stipulate that the IRB may still require that the PI provide the subject with a written statement about the research when granting a waiver of documentation.

  • Examples include mail out surveys or web based surveys. Or when the principal risk is a breach of confidentiality.

    45 CFR 46.117(c)

WAIVERS OF CONSENT

• Waiving the Consent Process:

  • Some research projects would not be possible if informed consent from subjects were required. The IRB may approve a consent procedure that does not include, or which alters, some or all of the elements of informed consent, or may waive the requirements to obtain informed consent.

  • Examples include retrospective chart reviews or analysis of existing specimens/records.

  • In order to grant this approval, it must be determined that the research is minimal risk and that adequate provisions are in place for protecting the confidentiality of the data.

    45 CFR 46.116(d)
UNANTICIPATED PROBLEMS

- Some Adverse Events qualify as Unanticipated Problems that must be reported to the IRB.
- An analysis is to be completed to determine if the Event/Problem is to be reported.
- UNANTICIPATED PROBLEM INVOLVING RISKS TO PARTICIPANTS OR OTHERS means any incident, experience, outcome, or new information where all three elements exist:
  - Is unexpected;
  - Is Related or Possibly Related to participation in the Research, and
  - It is indicated that subjects or others are at a greater risk of harm than was previously known or recognized.

UNANTICIPATED PROBLEMS

- *Time Frame for Reporting Unanticipated Problems:*
  - UPs are to be reported to the IRB promptly for review.
  - If the event requires immediate intervention to prevent serious harm to participants or others, the PI must report the event within *five (5) working days* of receiving notice of the event.
  - All other possible Unanticipated Problems are to be reported to the IRB as soon as possible but *no later than ten (10) working days.*
  - All communications from the Sponsor are to be submitted.

  SECTION 8 WITHIN THE HRPP SOPS
PROTOCOL DEVIATIONS & EXCEPTIONS

- The PI must notify the IRB of any Protocol Deviations or Exceptions that result in an increase in risk or a decrease in benefit to participants.

- A Protocol Deviation is a violation that occurs without any prior agreement.

- A Protocol Exception is a circumstance in which the specific procedures called for in the Protocol are not in the best interest of a specific subject; a violation that is anticipated and occurs with prior agreement.

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PROTOCOL DEVIATIONS & EXCEPTIONS

- *Time Frame for Reporting Protocol Deviations:*

- Any unplanned deviation from the Protocol must be reported to the IRB within ten (10) *working days* of learning of the deviation.

- If the Protocol Deviation has an impact on subject safety and/or may substantially alter the risks to subjects, these Deviations are to be reported within 48 *hours* of learning of the Deviation.

  SECTION 9 WITHIN THE HRPP SOPs
COMPLIANCE

- Non-compliance is a failure to comply with any of the regulations and policies described within the HRPP SOPs and failure to follow the determinations of the IRB. Non-compliance may be minor or sporadic or it may be serious or continuing.

- Serious non-compliance is the failure to follow any of the regulations and policies within the HRPP SOPs or failure to follow the determinations of the IRB and which, in the judgment of the convened IRB, increases risks to participants, decreases potential benefits, or compromises the integrity of the HRPP. Research being conducted without prior IRB approval is considered serious non-compliance.

- Continuing non-compliance is defined as a pattern of non-compliance that, in the judgment of the Research Compliance Officer or the convened IRB, suggests a likelihood that instances of non-compliance will continue without intervention. Continuing non-compliance also includes failure to respond to a request to resolve an episode of non-compliance.

COMPLIANCE

- Reporting Requirements:

- PIs and research staff are required to report instances of possible Non-Compliance.

- Reports of Non-Compliance must be submitted to the HRPO within ten (10) working days of discovery of the Non-Compliance. The report must include a complete description of the Non-Compliance, the personnel involved and a description of the Non-Compliance.

    SECTION 10 WITHIN THE HRPP SOPs
REGULATIONS & GUIDANCE

- In 1974, the National Research Act established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

- This Commission developed The Belmont Report which set forth the basic ethical principles that should underlie the acceptable conduct of research involving human subjects.

REGULATIONS & GUIDANCE

- *The Belmont Report:*
  - Respect for Persons: involves recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy
    * The need to obtain informed consent
  - Beneficence: entails an obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm
    * The need to engage in a risk/benefit analysis and minimize risk
  - Justice: requires that the benefits and burdens of research be distributed fairly
    * Requires subjects be selected fairly
REGULATIONS & GUIDANCE

- In response to the Commissions reports and recommendations, significant revisions were made to the DHHS and FDA Human Subjects Regulations.

  DHHS → 45 Part 46
  FDA → 21 Parts 50 and 56

TULANE HRPO

As a result of the process of Re-Accreditation, the Tulane HRPO has revised the following:

- SOPs
- Forms
- Letters
- Templates
- Website
OVERVIEW OF TULANE UNIVERSITY HRPP & GUIDANCE ON PROTECTING HUMAN SUBJECTS IN RESEARCH

PREPARATION FOR AAHRPP RE-ACCREDITATION SITE VISIT

As an Investigator/Researcher/Clinical Coordinator or part of research staff, you are an integral part of the Human Research Protection Program (HRPP) at Tulane University. Tulane University achieved accreditation for its HRPP on September 17, 2010 and is in the process of undergoing Re-Accreditation from AAHRPP. Achieving accreditation publicly affirmed Tulane University as a top-tier academic institution in its ethical and regulatory conduct of human subject’s research and hopes to maintain this achievement. AAHRPP accreditation is a gold standard that has contributed to increased interest in the research being performed at Tulane University.

The AAHRPP site review team will once again be on campus to conduct a site visit and will interview members of the HRPP.

AAHRPP Site Visit (MAY 29, 2013 - MAY 31, 2013)

Tulane University’s HRPP re-accreditation largely depends on these interviews. We are counting on the commitment you make to conduct quality research and solicit your help in this endeavor. To obtain re-accreditation, all interviews must be successful.

We have created materials to help you succeed and the IRB staff is also available for single or group prep sessions. The following guidance is not intended to be memorized; it is intended to focus your thinking as you prepare for the interview. The following items have been identified by other institutions as likely key areas of focus by the site review team:

- Know your roles(s) in the Human Research Protection Program
- Know the roles of other members of the HRPP
- Know where to obtain answers for ethical/regulatory behaviors expected of you in conducting research duties, (e.g. IRB SOPs, HRPP website, Research Policies)
- Know how to access IRB SOPs and Guidance, Research Policies
- Know how to report trouble, non-compliance, adverse events, unanticipated events, etc.
- Know where to go for advice (e.g. IRB Chair/Vice-Chairs, HRPO Staff, IRB Members)
- Compliant research records and documentation, and justification for decisions is expected
Focus on philosophical aspects of your role first, then know the regulatory details (e.g., the research you are performing is sound, purposeful and has value, before the nuts and bolts of compliance assessment)

- Understanding what constitutes a conflict of interest

- Describe the Human Subjects Education you’ve had, how you maintain compliance with GCP requirements (if conducting clinical trials) and how you use the education you’ve received in your research

- Understanding of the importance of the consent process

- Read the Belmont Report http://ohsr.od.nih.gov/guidelines/belmont.html
1. Do you know what AAHRPP accreditation is and why Tulane University is seeking it?

Tulane has applied for Human Subject Protection Program re-accreditation by the Association for the Accreditation of Human Research Protection Programs (AAHRPP) www.aahrpp.org. Steps 1 and 2 of the application process, which involve review of the policies, guidance and templates related to research, have been reviewed and accepted by the AAHRPP accreditation manager. As a measure of institutional commitment, accreditation site reviewers will be interviewing research investigators, staff and administration as part of the final process for accreditation.

AAHRPP’s Background

Responding to increased public and political scrutiny, AAHRPP seeks not only to ensure compliance, but to raise the bar in human research protection by helping institutions reach performance standards that surpass the threshold of state and federal requirements.

By establishing a "gold seal" signifying adherence to a rigorous set of human protection standards, accreditation by AAHRPP will help ensure consistency and uniformity among all institutions conducting biomedical, behavioral, and social sciences research.

AAHRPP’s Mission

The Association for the Accreditation of Human Research Protection Programs, Inc., (AAHRPP) works to protect the rights and welfare of research participants and promote scientifically meritorious and ethically sound research by fostering and advancing the ethical and professional conduct of persons and organizations that engage in research with human participants. AAHRPP achieves its mission by using an accreditation process based on self-assessment, peer review, and education.

Benefits of accreditation

Do the right thing: sound ethics in research...

Improves human research protection programs AAHRPP-accredited organizations make genuine, practical, and demonstrable improvements to their protection programs.

Improves research quality AAHRPP accreditation is based on the principle that human research protection is an integral component of a sound, quality-driven research program. When an organization earns accreditation, the global benchmark for research quality is raised.

Builds public trust AAHRPP accreditation indicates a "culture of concern"—a tangible demonstration to the public that an organization goes beyond minimal legal requirements in protecting research participants.

Get the advantage in regulatory compliance...

Assures regulatory compliance AAHRPP-accredited organizations achieve compliance with Department of Health and Human Services and Food and Drug Administration regulations, as well as other applicable regulations, such as Department of Energy or Department of Education
`Reduces burden from government and industry inspection` Routine audits from regulatory agencies and sponsors are less likely for accredited organizations. Government and industry can direct limited resources to organizations that have not yet demonstrated high quality through accreditation.

**Leads to better risk management programs** with increased liability, AHRPP accreditation reduces an organization's vulnerability due to non-compliance, and focuses attention on areas that need improvement.

**Gauges over-interpretation of regulations** AHRPP recognizes the "one-size-fits-all" protection model is not appropriate for all research types or settings. The accreditation process points out over-interpretation or mis-interpretation of regulations and helps organizations adjust accordingly.

**And get the competitive edge...**

**Makes your program more competitive** AHRPP accreditation provides a competitive advantage, indicating to sponsors that an organization values research protections, follows regulatory requirements, and has an efficient, streamlined protection system.

**Helps in recruiting participants** AHRPP accreditation assures interested individuals that the organization is committed to their well-being and puts their interests first.

**Attracts high-quality investigators** AHRPP accréditation signals to investigators the presence of a high-quality program—that scientific rigor and ethical standards are highly valued. Investigators can expect to find a competent IRB to review their research and an organization that will support them.

**Increases efficiency and reduces costs** through the self-assessment and external evaluation, AHRPP accreditation assists in streamlining operations, eliminating duplicative efforts, and reducing costs.

**Fosters alliances with accredited organizations** as the research enterprise moves in the direction of cross-disciplinary and collaborative research, AHRPP accreditation fosters partnerships among like-minded organizations.

2. **Tell us about the education you have completed regarding human subjects protection? Has your research staff completed human subject's education?**

All individuals involved in human subject's research at Tulane must complete the Collaborative IRB Training Initiative (CITI) modules as required by Tulane. In order to be listed on an IRB research application, all research investigators and staff must have completed the CITI training requirements. This is verified by the IRB office staff. In addition, Tulane requires human subjects training re-certification every 4 years. This can be accomplished by completing the CITI refresher course.

3. **What does the IRB do?**

There are two Institutional Review Boards at Tulane; a Biomedical IRB and a Social/Behavioral IRB. The IRB reviews and approves research in accordance with Department of Health and Human Services (DHHS) regulations in 45 CFR 46. For studies involving products regulated by the Food and Drug Administration (FDA), the IRB reviews research and comply with the requirements set forth in 21 CFR 50, 21 CFR 56, 21 CFR
112, 21 CFR 812. In addition, the IRB complies with HIPAA and its Regulations set forth in 45 CFR 160 and 164.

4. Do you know what minimal risk is and how it is evaluated?

According to the federal regulations, “minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.” Risk includes not only physical risk, but also psychological, emotional, legal, social, and financial. The definition of minimal risk serves as the starting point for the IRB’s determination of the category of review. If a project meets the definition of minimal risk, and falls into an exempt or expedited category, the Chair, Vice Chair, or designated IRB member may review and approve the project.

Any research study that if greater than minimal risk must be reviewed by the full IRB at a convened meeting.

5. Do you know the kinds and levels of risk?

A risk is a potential harm or injury associated with the research that a reasonable person in the subject’s position would likely be considered injurious. Risks can be categorized as physical, psychological, sociological, economic, and legal. Risks to subjects must be reasonable in relation to anticipated benefits, if any, to subjects and to the importance of knowledge that may reasonably be expected to result from the research.

Greater than Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Minimal risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. An example of minimal risk is the risk of drawing a small amount of blood from a healthy individual for research purposes (because the risk of doing so is no greater than the risk of doing so as part of a routine physical examination).

6. To whom do you go for help on issues, be they regulatory or ethical?

For assistance, you can contact the IRB; review the federal regulations, state and local laws, or colleagues.

7. What is the difference between privacy and confidentiality?

An issue of primary importance in the protection of human research subjects is the protection of privacy and confidentiality. Protection of Human Research Subjects privacy and confidentiality are extensions of the principles of autonomy (respect for persons) and beneficence from the Belmont Report.

Privacy can be defined in terms of having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.
"Confidentiality" pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others in ways that are inconsistent with the understanding of the original disclosure without permission.

IRB review of privacy and confidentiality protections is required under the Common Rule and the FDA regulations as well as state and local statutes. Protections to be reviewed by the IRB include promises to subjects on informed consents, protections during recruitment and follow-up, and methods to be employed to protect data and samples during storage, and use, and eventual data destruction (if promised). Sponsor access and any legally authorized access to subject information must be divulged in the consent form. Studies that obtain particularly sensitive information (e.g. HIV status, drug abuse) may be required to obtain a NIH Certificate of Confidentiality.

The IRB must decide on a case-by-case (e.g. study by study) basis whether there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. The IRB must take into account the degree of sensitivity of the information that may be obtained in the research and the protections offered the study and study population. As with other aspects of IRB review, these determinations will be dependent on the circumstances of the study and subjects.

Coded information, de-identified information and cultural differences in value systems must be understood by the IRB for study approval.

The investigator must describe plans to protect the subject's identity as well as the confidentiality of the research records. Care should be taken to explain the mechanisms that have been devised, for example, the use of numbering or code systems or safely locked files in private offices. Furthermore, the investigator should describe who has access to the data and under what circumstances a code system may be broken. Without appropriate safeguards, problems may arise from long-term retention of records. In special circumstances requiring additional safeguards to prevent potential criminal prosecution of the participating human subject, the IRB may require the destruction of all data that can identify the subjects. Subjects should be informed whether the data collected will be retained, and if so, for what purpose, what period of time, or whether and when data will be de-identified and destroyed.

A special situation arises for video or taped data and photographs since these media provide additional potential means for subject identification. Investigators must secure subject consent explicitly mentioning these practices. They should also explain plans for final disposition or destruction of such records.

8. What is the process of “consent”?

Obtaining informed consent is a basic ethical obligation for researchers. The process of consent should ensure that potential subjects are provided with information about the research project that is understandable by them, and permits the subject to make an informed and voluntary decision about whether or not to participate. The amount of information and the manner of presentation is generally related to the complexity and risk involved in the research study.

The Office for Human Research Protection provides a good description of the consent process.

http://www.hhs.gov/ohrp/
Informed consent is a process, not just a form. Information must be presented to enable persons to voluntarily decide whether or not to participate as a research subject. It is a fundamental mechanism to ensure respect for persons through provision of thoughtful consent for a voluntary act. The procedures used in obtaining informed consent should be designed to educate the subject population in terms that they can understand. Therefore, informed consent language and its documentation (especially explanation of the study’s purpose, duration, experimental procedures, alternatives, risks, and benefits) must be written in “lay language”, (i.e. understandable to the people being asked to participate). The written presentation of information is used to document the basis for consent and for the subjects’ future reference. The consent document should be revised when deficiencies are noted or when additional information will improve the consent process.

While the informed consent process is prospective and takes place prior to any research activity, consent should also be an ongoing educational interaction between the investigator and the research subject that continues throughout the study. It is not an exercise in persuasion. If an investigator has a relationship with potential subjects (physician-patient, instructor-student, employer-employee), care should be taken to avoid recruitment methods that may be seen as coercive due to the special relationship between parties.

Except in certain minimal risk studies, the Informed Consent Form is typically signed after the investigator has verbally explained the purpose and procedures involved in the study, answered questions, and otherwise provided information that permits the subject to make a prospective, informed decision. The Informed Consent Form must be signed before any study data collection procedures begin. The Informed Consent Form itself serves as a written source of information for the subject and documents the fact that the process of consent occurred.

Consent is a legal and ethical concept. Only legally competent adults can give legally effective informed consent. Minors and those individuals who are not competent to provide consent should be given the opportunity to assent to participate in the research project. Assent is an affirmative, knowledgeable agreement to participate in the project. Adequate provisions should be made for soliciting the independent, non-coerced assent from minors or cognitively-impaired persons who are capable of a knowledgeable agreement. In general, the IRB recommends that children ages seven and older be given the opportunity to assent.

9. What is the difference between waivers of consent and a waiver of documentation of consent? What justifies each?

In some situations, the IRB may waive the requirement for obtaining a signed Informed Consent Document (45 CFR 46.117(c)). Investigators may request that the IRB waive the requirement for a signed written informed consent. The IRB may waive the requirement for a signed consent if it finds:

a. The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality (the subjects would be placed at risk by documents linking them with an illegal or stigmatizing characteristic or behavior) or

b. The research presents no more than minimal risk of harm to the subjects and involves no procedures for which written consent is normally required outside of the research context.
In cases where the documentation requirement is waived the IRB may require the investigator to provide subjects with a written statement regarding the research.

Examples of types of studies that fall into the first category are survey or interview studies that contain highly sensitive (e.g., criminal behavior, sexual behavior) questions.

Examples of studies that fall into the second category are mail out surveys about topics that could not reasonably damage a participant's reputation or employability or be otherwise stigmatizing.

Waiver of documentation of consent may mean that no written document is provided to the subject at all, for example, in a random-dial telephone survey study. In this type of study, the telephone interview would begin with a script that includes all of the required elements of consent, but the study subjects would receive no written information about the study, either before or after the interview.

On the other hand, the waiver of documentation of consent may mean only that the subject's signature does not have to be obtained. The regulations stipulate that the IRB may still require that the investigator provide the subject with a written statement about the research when granting a waiver of documentation. For example, in a mailed-out survey study or in a web-based survey, the chair may determine that it is reasonable for the investigator to provide the subjects with an Information Sheet containing all of the basic elements of consent. The Information Sheet would simply have a statement that returning the survey or questionnaire via mail or the web or responding to the interview questions would constitute the subject's consent/agreement to participate in the research study.

**Waiver of Elements of Consent or Consent Itself**

Some research projects would not be possible if informed consent from subjects were required. The IRB may approve a consent procedure that does not include, or which alters, some or all of the elements of informed consent, or may waive the requirements to obtain informed consent. The IRB may consider waiving the requirement for some or all of the elements of informed consent (45 CFR 46.116(d)). The regulations state that informed consent may be waived in full or in part if the IRB determines that:

- the research involves no more than minimal risk to the subjects; and
- the waiver or alteration will not adversely affect the rights and welfare of the subjects; and
- the research could not practicably be carried out without the waiver or alteration; and
- whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Examples of types of studies in which all of the elements of consent have been waived include retrospective chart reviews, or studies of existing pathology specimens (all specimens to be studied have already been collected and are "on the shelf" at the time of the IRB application). Presuming that the study can be classified as minimal risk and that adequate provisions for protecting the confidentiality of the data are in place, the IRB generally finds that obtaining consent is impracticable (not possible).

If the investigator seeks a waiver of any or all of the elements of consent, the Initial Application Form should describe the reasons for the request, paying particular attention to why the research project would
The term "impracticable" means more than simple inconvenience - it means that the research could not be conducted without the waiver.

10. What are the criteria for reporting Unanticipated Problems or Protocol Deviations?

**Unanticipated Problems:**

**Section 8 within the HRPP SOPs**


Some adverse events qualify as unanticipated problems that must be reported to the IRB. Most adverse events do not.

Generally, an analysis of adverse event(s) that are serious (indicates that subjects or others are at a greater risk of harm than was previously known or recognized), related, and unexpected (all three) is the basis for concluding there is an unanticipated problem. These unanticipated problems must be reported to the IRB and sometimes require some change in the study (revised consent, protocol, or investigational brochure; stopping enrollment; terminating an arm of the study; etc.). These types of analyses are often done by Data Monitoring Committees or similar groups set up by the sponsor.

It is NOT helpful to human research subject protection to report all adverse events, especially minor, to the IRB. This practice takes up time that should be spent on the more important issues in protecting subjects and does not provide useful information to that end without additional analysis.

**Time Frame for Reporting Unanticipated Problems involving Risks to Subjects or Others**

PIs must report possible Unanticipated Problems to the IRB promptly.

If the event requires immediate intervention to prevent serious harm to participants or others, the PI must report the event within five (5) working days of receiving notice of the event.

PIs must report all other possible Unanticipated Problems occurring at the Tulane research site and non-Tulane research sites to the IRB as soon as possible but no later than ten (10) working days from the date of the event or from the date of being notified of the event.

Any and all communications with the study Sponsor must be submitted for review.

Unanticipated Problems are to be reported using the Unanticipated Problem Form within IRBNet.

**Local SAEs vs. External (non-local) SAEs**
To maximize subject protection, when local adverse events occur that are in the judgment of the investigator related + unexpected + serious (indicates that subjects or others are at a greater risk of harm than was previously known or recognized), you should report these along with the investigator opinion/analysis of whether this rises to the level of an unanticipated problem involving risks to subjects or others, and what if anything should change in the study.

To avoid taking valuable time away from more useful subject protection activities, please do not report external adverse events unless there has been an analysis or a judgment made that a particular adverse event or events that are related + unexpected + serious (indicates that subjects or others are at a greater risk of harm than was previously known or recognized) have created a signal that has been determined to be an unanticipated problem involving risks to subjects or others. Generally this will mean that something changes in the study (consent form, protocol, investigator brochure, stop enrollment, one arm will be closed, etc.). This type of analysis may be completed by the sponsor or a Data Monitoring Committee.

Protocol Deviations and Exceptions:

Section 9 within the HRPP SOPs

The Tulane IRB requires the reporting of protocol deviations or exceptions that result in an increase in risk or a decrease in benefit to participants.

A Protocol Deviation is a violation that is unanticipated and happens without any prior agreement from the sponsor or IRB.

A Protocol Exception is a circumstance in which the specific procedures called for in a protocol are not in the best interest of a specific patient/subject; a violation than is anticipated and happens with prior agreement from the sponsor.

Any planned deviation (Protocol Exception) from the protocol may be submitted to the IRB for review prior to implementation.

Time Frame for Reporting Protocol Deviations

Any unplanned deviation from the protocol must be reported within ten (10) working days of learning of the deviation.

If the Protocol Deviation has an impact on subject safety and/or may substantially alter the risks to subjects, such Deviations must be reported by the PI within 48 hours of learning of the Deviation.

Any and all communications with the study Sponsor must be submitted for review.

Protocol Deviations/Exceptions are to be reported using the Protocol Deviation & Exception Form within IRBNet.

.1. What is non-compliance, serious non-compliance and continuing non-compliance?
"complaints and Non-Compliance: Section 10 of the HRPP SOPs"

Non-compliance is a failure to comply with any of the regulations and policies described within the HRPP SOPs and failure to follow the determinations of the IRB. Non-compliance may be minor or sporadic or it may be serious or continuing.

Serious non-compliance is the failure to follow any of the regulations and policies within the HRPP SOPs or failure to follow the determinations of the IRB and which, in the judgment of the convened IRB, increases risks to participants, decreases potential benefits, or compromises the integrity of the HRPP. Research being conducted without prior IRB approval is considered serious non-compliance.

Continuing non-compliance is defined as a pattern of non-compliance that, in the judgment of the Research Compliance Officer or the convened IRB, suggests a likelihood that instances of non-compliance will continue without intervention. Continuing non-compliance also includes failure to respond to a request to resolve an episode of non-compliance.

**Reporting Requirements**

Investigators and their study staff are required to report instances of possible non-compliance.

Reports of Non-compliance must be submitted to the HRPO within ten (10) working days of discovery of this non-compliance. The report must include a complete description of the non-compliance, the personnel involved and a description of the non-compliance.

Examples of non-compliance that is to be reported to the HRPO:

- Failure to obtain IRB approval of human subject’s research when required
- Enrolling a research subject who does not fit the inclusion and exclusion criteria in the protocol
- Failing to obtain or document informed consent
- Administering a drug required by the protocol at a dose or schedule that has not been approved by the IRB except when necessary to eliminate apparent immediate hazards to the research participant.

The IRB will determine if a reported event constitutes serious or continuing noncompliance.


Modern human subjects protections begin with the *Nuremberg Code* developed for the Nuremberg Military Tribunal as standards by which to judge the human experimentation conducted by the Nazis. The Code captures many of what are now taken to be the basic principles governing the ethical conduct of research involving human subjects. The first provision of the Code states that “the voluntary consent of the human subject is absolutely essential.” Freely given consent to participation in research is thus the cornerstone of ethical experimentation involving human subjects. The Code goes on to provide the details implied by such a requirement: capacity to consent, freedom from coercion, and comprehension of the risks and benefits
involved. Other provisions required the minimization of risk and harm, a favorable risk/benefit ratio, qualified investigators using appropriate research designs, and freedom for the subject to withdraw at any time. Similar recommendations were made by the World Medical Association in its Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects, first adopted by the 18th World Medical Assembly in Helsinki, Finland, in 1964, and subsequently revised by the 29th World Medical Assembly, Tokyo, Japan, 1975, and by the 41st World Medical Assembly, Hong Kong, 1989, and by the 52nd World Medical Assembly, Edinburgh, Scotland, 2000 (note of clarification on paragraph 29 added by World Medical Assembly, Washington, DC, 2002). The Declaration of Helsinki further distinguishes therapeutic from non-therapeutic research.

In the United States, regulations protecting human subjects first became effective on May 30, 1974. The regulations established the IRB as one mechanism through which human subjects would be protected.

In July of 1974, the passage of the National Research Act established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission met from 1974 to 1978. In keeping with its charge, the Commission issues reports and recommendations identifying the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and recommending guidelines to ensure that research is conducted in accordance with those principles. The Commission's report setting forth the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects is titled The Belmont Report, and is discussed in depth below.

In 1981, in response to the Commission's reports and recommendations, both the Department of Health and Human Services and the FDA promulgated significant revisions of their human subject's regulations. They are concerned with some of the details of what the IRB is expected to accomplish and some of the procedures it must follow.

The DHHS regulations are codified at Title 45 Part 46 of the Code of Federal Regulations. Those "basic" regulations became final on January 16, 1981, and were revised effective March 4, 1983, and June 18, 1991. The June 18, 1991, revision involved the adoption of the Federal Policy for the Protection of Human Subjects. The Federal Policy (or "Common Rule," as it is sometimes called) was promulgated by the sixteen federal agencies that conduct, support, or otherwise regulate human subject's research; the FDA also adopted many of its provisions. As is implied by its title, the Federal Policy is designed to make uniform the human subject's protection system in all relevant federal agencies and departments that adopt it.

Additional protections for various vulnerable populations have been adopted by DHHS, as follows:


Subpart C, "Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects" became final on November 16, 1978.

Subpart D, "Additional Protections for Children Involved as Subjects in Research" became final on March 8, 1983, and was revised for a technical amendment on June 18, 1991.
FDA regulations on the protection of human subjects are codified at Title 21 Parts 50 and 56 of the Code of Federal Regulations. Part 50, which sets forth the requirements for informed consent, became final on May 30, 1980, and was revised effective January 27, 1981, March 3, 1989, and June 18, 1991. Subpart C, which provides special protections for prisoners, was adopted on July 7, 1981; the effective date of Subpart C has stayed until further notice. Subpart D, Additional Safeguards for Children in Clinical Investigations, was adopted effective April 24, 2001. Part 56, which sets forth the provisions for institutional review boards, was adopted on January 27, 1981, with revisions to some sections effective February 27, 1981, March 3, 1989, and June 18, 1991.

Additional FDA regulations that are relevant to IRB review of research are Parts 312 (Investigational New Drug Application), 812 (Investigational Device Exemptions) and 860 (Medical Device Classification Procedures).

Belmont Report

On September 30, 1978, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research submitted its report entitled The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. The Report sets forth the basic ethical principles underlying the acceptable conduct of research involving human subjects. Those principles, respect for persons, beneficence, and justice, are now accepted as the three quintessential requirements for the ethical conduct of research involving human subjects.

Respect for persons involves recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy.

Beneficence entails an obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm.

Justice requires that the benefits and burdens of research be distributed fairly.

The Report also describes how these principles apply to the conduct of research. Specifically, the principle of respect for persons underlies the need to obtain informed consent; the principle of beneficence underlies the need to engage in a risk/benefit analysis and to minimize risks; and the principle of justice requires that subjects be fairly selected. As was mandated by the congressional charge to the Commission, the Report also provides a distinction between “practice” and “research.” The text of the Belmont Report is thus divided into two sections: (1) boundaries between practice and research; and (2) basic ethical principles. The full text of the Belmont Report should be read by all those who are part of the Tulane Human Subjects Protection Program. The Belmont Report is available on the IRB website.
ADDITIONAL QUESTIONS FOR PRINCIPAL INVESTIGATORS AND RESEARCH STAFF:

- How are you trained to do your job?
- What do you consider your primary responsibility in conducting a human research study?
- What are your job responsibilities?
- Who completes the IRB Application(s)/submissions?
- How does the research team work together?
- What are your complaints about IRB submission and the review process?
- Your workload vs. your resources, overwhelming?
- Discuss the research study/studies that you are currently working on. What is the purpose of the research? What are the procedures? What drugs are being used? How are subjects approached? Who consents the subjects?
- How do you consider protecting study participants?
- How do you find out details about the study protocol?
- What happens when a subject withdraws from a study?
- Describe the consent process, where does it take place, how long does it last, does the subject get a signed copy of the Consent Form?
- What would you do if you had a potential subject that could not speak English?
- Is there a 24 hour contact number for subjects to reach research staff?
- How do you handle complaints about the study?
- How do you handle Unanticipated Problems?
- How soon do you submit a report to the IRB if something goes wrong?
Summary of Revised HRPP/HRPO Documents

Revised Policies

*Please Note: The revised Policies are now on the HRPO Website under the Policies tab. The Full Version is the revised version.

1. DOD-DON Policy
2. ICH-GCP Policy
3. HRPO/HRPP Policy
   a. Section 3 – IRB Review Process (substantial changes)
   b. Section 5 – Obtaining Informed Consent from Research Subjects (substantial changes)
   c. Section 6 – Vulnerable Subjects in Research
   d. Section 7 – FDA-Regulated Research (e.g., Investigational Drugs & Devices in Research) (substantial changes)
   e. Section 8 – Unanticipated Problems Involving Risks to Subjects or Others (substantial changes)
   f. Section 9 - Protocol Deviations and Exceptions (substantial changes)
   g. Section 12 - Investigator Responsibilities (substantial changes)
   h. Section 13 – Sponsored Research (substantial changes)
   i. Section 14 – Conflicts of Interest in Research - All conflict of interest (COI) matters must be resolved before the IRB can act to approve a submission. This includes COI issues that relate to PIs, investigators, and key personnel. To be safe, investigators should resolve all COI issues before making a submission to the IRB.
   j. Section 17 – Collaborative Research and Off-Site Research (substantial changes)
   k. Section 18 – Special Topics (substantial changes)

Applications/Forms were revised per AAHRPP suggestions

1. Application Part 1
2. Exempt Application
3. Application Part 2 for Expedited & Full Board Studies
4. Continuing Review Form
5. Amendment Form
6. Protocol Deviation & Exception Form
7. Unanticipated Problem & Reportable Event Form
8. Closure Form
Templates & Checklists were revised per AAHRPP suggestions

1. Biomedical Consent Template
2. Social/Behavioral Consent Template
3. Initial Submission, Secondary Submission & Exempt Checklists
4. All HRPO Letter Templates have been revised

Supplements were revised per AAHRPP suggestions

1. All Supplements
2. Supplement N (Conflict of Interest) was significantly revised
3. There is a new Supplement to request a waiver of HIPAA

Reviewer Sheets were revised per AAHRPP suggestions

1. Initial Submission Reviewer Sheet for Biomedical Researchers
2. Initial Submission Reviewer Sheet for Social/Behavioral Researchers
3. Continuing Review Reviewer Sheet

Other Misc. Forms were revised per AAHRPP suggestions

1. Clinical Trial Agreement Checklist (ORA Form)
2. Submission and Routing of Proposals for Extramural Funding and Award Acceptance Policy
3. Disaster Planning for Biomedical Subject Safety