CLINICAL COORDINATORS SEMINAR:
10/19/2010 and 10/21/2010

AGENDA:
- NAVIGATING THE TULANE HRPP WEBSITE
- IRBNet VIDEO AND ADVANCED TOPICS
- IRB SUBMISSIONS: COMMON ISSUES WITH INITIAL SUBMISSIONS, CONTINUING REVIEWS, ETC. (Ashley Tillison, MSPH)
- RESEARCH PHARMACY PROCESS OVERVIEW
  (Ricky George, PharmD.)
- CLINICAL COORDINATORS TRAINING INTRODUCTION
  (Roberta McDuffie, MSN)
- TULANE MEDICAL CENTER IRB PROCESS
  (Michele Pomes, RN)
- CONFLICT OF INTEREST COMMITTEE SUBMISSION PROCESS
  (Genean Mathieu, BA)
- OFFICE OF RESEARCH ADMINISTRATION/GRANTS & CONTRACTS
  (Linda Hardy, MSW)

Tulane HRPP Website

- The website address is: http://tulane.edu/asypr/irb
  *Please note www.irbnet.org is NOT the HRPP website. IRBNet is our electronic submission system and it is independent of Tulane.
IRB Submissions

Common Problems Include:

1. Beware of copying and pasting to Applications directly from the protocol. Make sure that you are responding to the question and giving a COMPLETE and CONCISE answer.

2. Make sure the information presented in all documents is consistent.

3. Make sure your cover letter not only lists what is included in your submission but also an explanation regarding any items that are missing and/or if any special considerations are needed for your approval letter.

4. For unanticipated problems and protocol deviations, if there is no communication to and/or from the sponsor regarding the deviation or problem please indicate that on your cover letter. Please note section 8 and 9 of the SOPs for guidance regarding unanticipated problems and protocol deviations. These sections of the SOPs are included in this packet for your convenience.

5. Please utilize the initial and secondary submission checklists to be sure that you are submitting all necessary documents.

6. For amendments please be sure to submit a clean version and marked version of revised documents.
IRB Submissions

7. Initial application part 1 must be completed for ALL studies. Please see the IRBNet User's guide for instructions on how to locate it.

8. For exempt studies, a data collection tool is required that lists specifically what data you are collecting. e.g. height, weight, age, diagnosis

9. FOR INITIAL SUBMISSIONS, the electronic signature of the PI and Department Head through IRBNet is required. If the PI is the Department Head, the PI and the Dean are required to sign. If the PI is the Dean, the PI and the VPR are required to sign. If the PI is a student, the PI and Faculty Advisor is required to sign in lieu of the Department Head.

10. FOR ALL OTHER SUBMISSIONS, electronic signature of the PI ONLY through IRBNet is required.

IRB Submissions

11. A submission that is a response to a deferral is NOT an initial submission nor is it an amendment. Therefore the department head or deans signature is not required and you should not include an application for amendment.

12. Any participant recruitment conducted off-site or any research procedures performed off-site (i.e. clinics or organizations, etc.) require agreement from that the site where the recruitment of research procedures are performed.

13. When you receive a deferral letter or information required letter the proper response is to create a new package NOT have your submission unlocked. The new package should include a detailed cover letter addressing each issue from your deferral or information required letter point-by-point along with any new or revised documents included.
Cover Letter (Incorrect)

[DATE]
TO: Tulane University Human Research Protection Program
RE: Protocol #2010 - A Phase II, Randomized, Double Blind, 2-Way Crossover Safety and Efficacy Study of Insulin in Patients with Type 2 Diabetes

PRINCIPAL INVESTIGATOR: Ashley S. Tillison, MSPH
STUDY COORDINATOR(S) (if applicable): [LIST COORDINATOR(S) HERE]
Enclosed please find the following documents for a/an [SUBMISSION TYPE]:
1. CITI Training Certificates
2. Protocol
3.
4.
5.

[ADD ADDITIONAL INFORMATION OR ANY DETAILS FOR HRPO STAFF/REVIEWER HERE]
[IF THERE IS ANY PARTICULAR LANGUAGE THAT YOU REQUIRE ON YOUR APPROVAL LETTER, DESIGNATE THAT LANGUAGE HERE]

Cover Letter (Correct)

October
TO: Tulane University Human Research Protection Program
RE: Protocol #2010 - A Phase II, Randomized, Double Blind, 2-Way Crossover Safety and Efficacy Study of Insulin in Patients with Type 2 Diabetes

PRINCIPAL INVESTIGATOR: Ashley S. Tillison, MSPH
STUDY COORDINATOR(S) (if applicable): N/A
Enclosed please find the following documents for a Initial Submission:
1. CITI Training Certificates
2. Protocol
3. Survey
4. Supplement H
5. Initial Application part 1 and Initial Application part 2

IT not included with submission because study sponsor is not providing funding.
Initial Submissions

3. Review Type Requested:  
- Biomedical  
- Social/Behavioral  
- Expedited  
- Convened IRB

*Please pick the two most appropriate answers.
6. **Research Description (CORRECT)**

a. Please provide a brief (less than 1 page) summary of the background information for this research study in language that can be understood by a non-scientist.

When a healthy person starts to eat, there is a rapid insulin response. Currently available injectable insulin products do not replicate the natural insulin response to a meal challenge. Instead, injectable insulins enter the bloodstream relatively slowly, and, likewise, they tend to have a duration of action that is too long for the desired outcome. As a consequence, patients with diabetes have inadequate levels of insulin present at the initiation of a meal and very often have too much systemic insulin between meals. This may lead to hyperglycemia in the early post-meal time period, followed by risk of hypoglycemia between meals.

In pursuit of this clinical development program, Tulane Pharmaceuticals performed a single Phase 1 study in volunteer subjects to determine the time-concentration profile of Insulin 1 and Insulin 2 in combination with adjuvant along with measures of glucose control. The co-injections demonstrated a significantly faster absorption of insulin and greater peak insulin levels along with corresponding acceleration of insulin action compared to the existing, marketed formulations of these two insulins.

Other clinical studies of insulin coadministered with study adjuvant demonstrated insulin kinetics that better replicate the natural insulin response to a meal in healthy individuals. Specifically, coadministration of insulin with adjuvant accelerates the onset of insulin action, the time of peak insulin concentration, and the offset of insulin action. In healthy volunteers, this acceleration of insulin exposure results in accelerated glucose metabolism. In patients with Type 1 and Type 2 diabetes mellitus, the acceleration of insulin exposure has been shown to reduce postprandial hyperglycemia, as measured by peak blood glucose, two-hour postprandial glucose, and total area of glucose excursions >140 mg/dl occurring in response to a standardized liquid test meal. Building on 'Tulane Pharmaceuticals’ experience with adjuvant co-injected with insulin products, this Phase 2 study is designed to demonstrate non-inferiority of Insulin 2 or Aspart-PHP20 to Insulin 2 alone, with respect to glycemic control as assessed by changes in A1C in patients with Type 2 diabetes mellitus.

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b. Describe the specific scientific objectives of the proposed research in language understandable to the IRB committee members (less than 1 page). The IRB is comprised of scientists with varied backgrounds, non-scientists, and community members. (CORRECT)

**Primary Objective**

- To demonstrate non-inferiority of Insulin 2 or Aspart-PHP20 to Insulin 2 alone with respect to glycemic control, as assessed by change in A1C from baseline.

**Secondary Objectives**

- To compare Uspro-PHP20 to Insulin 2, Aspart-PHP20 to Insulin 2, and combined results for Aspart-PHP20 and Uspro-PHP20 to those for Insulin lispro, with respect to postprandial glucose changes from pre-meal baseline.
- To compare combined results for Aspart-PHP20 and Uspro-PHP20 to those for Insulin 2, with respect to the following:
  - Change in A1C from baseline.
  - Proportion of patients achieving or maintaining A1C < 7.0% and, separately, A1C ≤ 6.5%.
  - Overall rate of hypoglycemia as defined in Section 11.6.

**Exploratory Objectives**

- To compare Uspro-PHP20 to insulin 2 and Aspart-PHP20 to insulin 2 with respect to:
  - Change in A1C from baseline.
  - Proportion of patients achieving or maintaining A1C < 7.0% and, separately, < 6.5%.
  - Overall rate of hypoglycemia as defined in 11.6.
To compare lispro-PH20 to Insulin 2, Aspart-PH20 to Insulin 2, and combined results for Aspart-PH20 and Lispro-PH20 to those for Insulin 2 with respect to:

- Rates of severe hypoglycemia as defined in Section 11.6.
- Rates of nocturnal and postprandial hypoglycemia.
- Rates of total, nocturnal and postprandial hypoglycemia after adjustment for differences in A1C.
- Attainment of pre-specified postprandial blood glucose (PPG) targets (e.g. two-hour PPG <140 mg/dL and peak PPG <180 mg/dL).
- Glucose control as shown by blinded continuous glucose monitoring (CGM) calibrated with finger stick blood glucose measurements (e.g. percent of time within prespecified target range, percent of time above or below prespecified target values).
- Levels of 1,5-anhydroglucitol (1,5-AG), determined by Glycomark assay, during each treatment period.
- Prandial insulin dose at each meal, total prandial, total basal and total daily insulin doses.
- Variability of glucose measurements, within patient and between patients.
- Weight changes during each treatment period

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c. Describe the research procedures that will be followed. Identify all procedures that will be carried out with each group of subjects. Describe study participant procedures including: how often will study visits occur; and for how long? Will machinery, equipment, and/or instruments be used? If so, please list and describe their use.

Suggestions:

1. Create a bulleted list of study procedures. Next to each procedure state which study visit(s) during which the procedure will occur.

2. Create a chart of study procedures.

3. Explain study procedures that are not common or that may be confusing.

4. DO NOT cut and paste lengthy and technical language from the protocol

* The goal: Your research procedures should be COMPLETE BUT CONCISE!
### 3. STUDY SCHEDULE OF EVENTS

#### Table 1: Study Schedule of Events

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<th>Visit</th>
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### Table 2: Schedule of Events

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**Notes:**
- All specified procedures will be done at V1, V2, V3, and V22, except for study drug administration. Therapy drug will be given during V19-21 days of the protocol. As for V19-21, the study drug will be given for the patient's blood pressure or the assumed period of the main study protocol. All other parameters will be monitored on a 24-hour basis.
- The study drug will be given for the entire period of the protocol. The study drug will be given at V19-21 days of the protocol.
- The study drug will be given during the entire period of the protocol. The study drug will be given for the entire period of the protocol.
8c. Is this a multi-center study?  ✔ Yes  ❌ No.

If Yes,
Are you the Lead Investigator?:  ✔ Yes  ❌ No
Is Tulane the Lead Site?:  ✔ Yes  ❌ No

If either of the above is Yes, describe provisions for the management of information obtained from the different sites that might be relevant to the protection of participants:

*Multi center research is research that is performed at many different sites, domestic and/or international, and this research is guided by a central research organization or pharmaceutical company. The research is performed by different PIs at each site and the PI is usually affiliated with the site that the research is being performed at.

E.g. A cancer drug trial sponsored by the NCI or A cardiovascular drug trial sponsored by Novartis.

*Collaborative research is performed at different sites that are not affiliated with Tulane and is guided by one Tulane PI.

E.g. A study assessing the quality of care at several free health clinics in New Orleans led by John Doe, MD, a Tulane PI.

A letter of cooperation or approval must be submitted from each site granting permission for recruitment and/or conduct of research at those sites.

10c. Indicate the recruitment method for finding potential participants:

✔ Telephone Calls
✔ Contact Letters
✔ Brochures – Will be... posted ✔ mailed ✔ hand distributed
✔ Flyers – Will be... posted ✔ mailed ✔ hand distributed
✔ Advertisement –

Will an advertising company be employed for recruitment purposes?  ✔ Yes  ❌ No
If yes, please specify the company and the service they will be providing:

✔ Internet – Please specify the web site addresses:
   ✔ Other, please describe:

*If participants are being recruited from the PI's patient population the appropriate answer is Other, please describe.
* Do Not check any of these recruitment methods if the supporting documents are not included in your submission.
11 b. If subjects will be paid or receive any sort of compensation for participation in research, please describe the compensation, the distribution strategy, and what will happen if the subject chooses or must discontinue participation during the study. (Payment or compensation cannot be contingent upon the completion of the entire study.)

*Please state:
1. Which study visits participants will be paid for?
2. How often participants will be paid?
3. How much will participants be paid?
4. How much will participants be paid if they don’t complete the study (prorating)?
5. If foreign currency is being used please state the exchange rate.
6. What is the form of the compensation? e.g. check, gift card, food
7. If compensation will be given in the form of a gift, what is the value of that gift?

(Correct)
13. Risks:

Note: According to NIH Regulations minimal risk means "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."

a. If the classification is minimal risk, please justify why that category is appropriate and then skip to the Section on Benefits:

N/A

b. If the classification is greater than minimal risk, describe all of the risks (including non-physical risks) in detail and assess their seriousness.

Hypoglycemia, a condition that occurs when your blood sugar (glucose) is too low and which is a well known risk of insulin treatment and patients will already have been educated on its prevention and treatment

c. What precautions have been taken to minimize these risks and what is their likely effectiveness?

Education

d. Describe other alternative and accepted procedures to minimize risk, if any, that were considered and why they will not be used.

None available
14. Benefits:

a. Assess the potential benefits to science and/or society which may accrue as a result of this research.

Novel way to enhance insulin absorption which is a problem in practice

b. Are there any benefits which may accrue to the individual subjects in this research?

☐ Yes ☐ No  If yes, please explain:

c. If the risk in this study is more than minimal, explain how the risks are reasonable in relation to the benefits:

Diabetes control in general is poor and most patients do not achieve normal blood sugars all the time

* Do Not leave any questions blank. Please state if a question is not applicable and give a justification for why the question is not applicable.

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Initial submissions

• Use the initial submission checklist to determine what documents are required for ALL initial submissions including exempt initials, expedited initials and full board initials.

• Use the IRBNet User’s Guide, located on the IRBNet Hub on the homepage of our website (right side) for instructions on how to submit your initial submission through IRBNet.

• To determine what type of review your study qualifies for please see the investigator guidance link on our website and look at the criteria for review documents.

• For questions about submissions in general please email us at irbmain@tulane.edu
• Please note that supplements are attached to Initial application part 2. Please do not fill out the supplements as a separate document unless you are not completing Initial application part 2 as part of your submission.

• Make sure CITI Training certificates are included with EVERY Initial submission and Continuing Review submission for ALL study team members listed on Initial Application part 1 and the Consent form.
2. Specify the Study's Current Status Below – Note: If all research-related activities have been completed, the study has been terminated, or the study was never initiated, use the “Study Closure Form."

- Enrollment has not yet begun
- Enrollment is in progress
- Closed to enrollment but contact with the participants is ongoing (any interventions, treatments)
- Closed to enrollment but follow-up of subjects continues
- Closed to enrollment but data analysis continues

*Choose only one status.

3. Funding Status – Note: Submit the grant proposal or contract if not on file with the IRB

- Project is currently funded: Funding Agency (e.g. NIH):
  Grant/Contract Number:
- No Funding Obtained or Applied For.
- Project has been submitted for funding: Industry-Sponsored Funding Agency (e.g. NIH):

* e.g. by definition means “for example”. There are many different funding agencies other than the NIH. If your study has a funding agency you should list it next to Funding Agency (e.g. NIH):
17. Since the last IRB review, have there been any problems with or any changes to the research (including the following: subject recruiting, advertising, subject compensation, inclusion or exclusion criteria, costs to subjects, consent process, documentation of informed consent, privacy or confidentiality, safety monitoring, subject populations, etc.)? If Yes, please provide a summary of the problems/changes.

*If you submit ANY revised documents with your continuing review you should answer this question. An amendment form is not necessary if this question is answered.

25. If there has been a lapse in IRB Approval, what research-related activities have occurred during the period for which there was no IRB approval?

*You should answer this question if you are submitting your continuing review after the expiration date and within the 30 day lapse period.

---

**Continuing Reviews**

- If your study is greater than minimal risk and there are no updated DSMB or DSMC reports please indicate that on your cover letter.

- If you include a DSMB or DSMC report with your submission please be sure it includes information regarding the study in question.

- Make sure CITI Training certificates are included with EVERY Initial submission and Continuing Review submission for ALL study team members listed on Initial Application part 1 and the Consent form.
1440 Canal Street, Suite 1705, TW-36
New Orleans, LA 70112-2669
504-988-2665
Email: irbmain@tulane.edu
Web: http://tulane.edu/asvpr/irb
Tulane University Human Research Protection Program
Application for Human Subjects Research
For Expedited and Convened IRB Studies

Sponsored and Un-sponsored Research

Prior to commencing any research involving human subjects, investigators must complete and submit this application to Tulane’s Human Research Protection Office through IRBNet. Prior to submitting this application these additional requirements must be met:

- **CITI Training**: All research personnel conducting human subjects’ research **must** complete the mandatory CITI Training course online at [www.citiprogram.org](http://www.citiprogram.org), which can be accessed through the Tulane HRPO website, [http://tulane.edu/asypr/irb](http://tulane.edu/asypr/irb).
- **Conflict of Interest Form**: All Tulane Faculty and Staff must complete a Conflict of Interest Disclosure Form found at [http://coi.tulane.edu](http://coi.tulane.edu). Please **DO NOT** submit the form to the HRPO.
- **International Research**: If any aspect of the research involves international activities (i.e., travel outside of the U.S., the import or export of items into or out of the U.S. or the involvement of foreign nationals), then the International Projects Preliminary Questionnaire must be completed. This form is available at [http://www.som.tulane.edu/researchadmin/IPPQ.htm](http://www.som.tulane.edu/researchadmin/IPPQ.htm). Please **DO NOT** submit the form to the HRPO.
- **Industry Sponsored Research**: If the research project is industry-sponsored (e.g., pharmaceutical sponsor), then an Interdepartmental Order form must be completed and submitted with the $2,500 IRB initial application fee. The IT form can be found at [http://www.tulane.edu/~tams/forms/forms/itforms.htm](http://www.tulane.edu/~tams/forms/forms/itforms.htm).
- **ICH-GCP Requirements**: All clinical trials (both domestically and internationally) must comply with the International Conference on Harmonization (ICH) Good Clinical Practices (GCP) requirements found in section E6. For additional guidance, refer to Tulane’s policy entitled “International Conference on Harmonization (ICH) Good Clinical Practices (GCP), Applicability to Human Subjects Research”
- **Submission of this Form**: When you have completed this form, please submit it to the HRPO through IRBNet at: [https://www.irbnet.org/](https://www.irbnet.org/)

*Note: If the protocol is a clinical trial, a copy of this completed form, together with a copy of the Clinical Trial Agreement should be submitted to the Office of Research Administration (ORA).*
1. **Protocol Title:**

2. **Principal Investigator:**

   Name:  
   Email:  

   *Note: The electronic signature of the Department Head is required for all Convened and Expedited Biomedical and Social/Behavioral Initial Submissions in addition to the PI electronic signature except for Student PIs where the electronic signature of the Faculty Advisor is required.*

   a. Describe the process used to ensure that all persons assisting with the research have been adequately informed about the protocol and describe each person’s role in the project.

3. **Review Type Requested:**

   - [ ] Biomedical
   - [ ] Social/Behavioral
   - [ ] Expedited
   - [ ] Convened IRB

   *Note: To request exemption status, submit the Exemption Application Form. To find guidance concerning the categories of research (Exempt, Expedited, or Full Board), consult our website at [http://tulane.edu/asvpr/irb](http://tulane.edu/asvpr/irb).*

4. **Funding Information:**

   a. Please provide one complete copy of the Grant/Contract Proposal and the Grants and Contracts Routing Form, if applicable. Please note that submission of your grant application is a regulatory requirement and will be maintained for the record with your application. The IRB will not utilize the grant during the review process other than to confirm that the grant proposal is consistent with the IRB protocol. If the research project is industry-sponsored (e.g., pharmaceutical sponsor), then an Interdepartmental Order form must be completed and submitted with the $2,500 IRB initial application fee. The IT form can be found at [http://www.tulane.edu/~tams/forms/forms/itforms.htm](http://www.tulane.edu/~tams/forms/forms/itforms.htm).

5. **Conflict of Interest:**

   a. Do any members of the research team or any of their immediate family members have any financial interest in the sponsor of this research and/or in the results of this research?  
   - [ ] Yes  
   - [ ] No

   If Yes, please contact Genean Mathieu, Administrative Compliance Specialist for the University Conflict of Interest Committee at 504-247-1286 or via email at gmathieu@tulane.edu.

   b. Is there a protocol-specific Conflict of Interest?  
   - [ ] Yes  
   - [ ] No

   If Yes, **Complete IRB Supplement N.**

6. **Research Description:**

   (space for text)
a. Please provide a brief (less than 1 page) summary of the background information for this research study in language that can be understood by a non-scientist.

b. Describe the specific scientific objectives of the proposed research in language understandable to the IRB committee members (less than 1 page). The IRB is comprised of scientists with varied backgrounds, non-scientists, and community members.

c. Describe the research procedures that will be followed. Identify all procedures that will be carried out with each group of subjects. Describe study participant procedures including: how often will study visits occur, and for how long? Will machines, equipment, and/or instruments be used? If so, please list and describe their use.

d. Describe the data to be collected, the source of the data and the data collection procedures

    Note: Upload copies of all questionnaires, surveys, interview questions, etc. If the research involves interviews that could evolve as the research progresses, include a list of discussion topics and any “starter” questions for each topic that can reasonably be expected to be covered. If a draft of a written questionnaire or survey is attached, it should be clearly labeled as such and a final version must be submitted before data collection begins.

7. Adequacy of Resources to Protect Subjects:

   a. Investigator (including co-investigators) has sufficient time to conduct and complete the research. □ Yes □ No

   b. Adequate qualified (including experience, training and familiarity with the protocol) staff are available for this research. □ Yes □ No

   c. Does your study involve any of the following physiological processes? □ Yes □ No
      • Collection of blood samples through venipuncture
      • Collection of biological samples (e.g., sweat, urine, saliva, sputum)
      • Physiological monitoring (e.g., EEG, EMG)
      • Exercise or stress tests
      • Medical imaging (e.g., MRI, fMRI, PET)
      • Administration of alcohol or drugs

      If Yes, Complete IRB Supplement I.

   d. Describe availability of psychological, social or medical services, including counseling or social support services that may be required as a consequence of research participation. If none are available, what provisions are made when necessary)
e. Describe psychological, social or medical monitoring, ancillary care, equipment that might be needed to protect participants.

f. Describe other resources needed for the protection of subjects in the conduct of this research (e.g. participant communication needs language translation services.)

g. Explain how the Investigator has access to a population that would allow recruitment of the required number of subjects.

8. Location Information:

a. Describe the settings in which research procedures will be carried out (e.g., hospital, clinic, school, home, lab, etc.).

b. List all non-Tulane sites where the procedures will be carried out. For each site, describe the IRB communication with the external site and indicate whether the site has an IRB, whether the site has granted permission for the research to be conducted, and the contact information for the site.

c. Is this a multi-center study? □ Yes □ No.

If Yes,
Are you the Lead Investigator?: □ Yes □ No
Is Tulane the Lead Site?: □ Yes □ No

If either of the above is Yes, describe provisions for the management of information obtained from the different sites that might be relevant to the protection of participants:

d. Please complete the table below for all research sites.

Note: Host community approval is required and final IRB approval is contingent upon receipt of this approval.

<table>
<thead>
<tr>
<th>Name of Research Site:</th>
<th>IRB Approval</th>
<th>Letter of Cooperation if site has no IRB</th>
</tr>
</thead>
</table>

4
9. **Study Population:**

   a. Age range of participants:

   b. Total number of participants stated in the protocol to be studied at all sites (regardless of PI)?

   c. Total number of participants that are to be studied at all Tulane University sites:

   d. In the chart below, please estimate the number of participants to be consented at Tulane:

<table>
<thead>
<tr>
<th>Adults</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minors (under age 18)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

   *Note: If research involves children, please complete Supplement A.*

   e. What are the research subject inclusion/exclusion criteria regarding gender, age, race, ethnicity, and other criteria? If you plan to target a particular gender, races, and/or ethnicity to the exclusion of others, please provide an explanation.

   f. Does your study population include Tulane University Students and/or Employees?

   □ Yes □ No

   If Yes, explain the involvement of the students/employees:
10. Recruitment Information:

a. Where will subjects be recruited? Describe how prospective subjects will be identified and contacted.

b. Who will approach and/or contact prospective research subjects?

c. Indicate the recruitment method for finding potential participants:

☐ Telephone Calls
☐ Contact Letters
☐ Brochures – Will be...
☐ Flyers – Will be...
☐ Advertisement –

☐ posted ☐ mailed ☐ hand distributed
☐ posted ☐ mailed ☐ hand distributed

Will an advertising company be employed for recruitment purposes? ☐ Yes ☐ No
If yes, please specify the company and the service they will be providing:

☐ Internet – Please specify the web site addresses:
☐ Other, please describe:

Note: All Recruitment Materials (including advertisements, flyers, any recruitment letter/emails sent to subjects, etc.) must be submitted to the IRB for review with this application before implementation.

If your recruitment method or any aspect of your research involves the Internet, complete Supplement F within this Application.

11. Payment and Compensation Methods:

a. Will any payment or compensation (e.g. course credit) be offered to the participants for their participation?

☐ Yes ☐ No

b. If subjects will be paid or receive any sort of compensation for participation in research, please describe the compensation, the distribution strategy, and what will happen if the subject chooses or must discontinue participation during the study. (Payment or compensation cannot be contingent upon the completion of the entire study.)

Note: A statement must be included within the informed consent document explaining how compensation will be handled in the event the participant withdraws from the study.
c. If subjects will be charged for research-related procedures or any additional costs are anticipated, please describe.

*Note: Any financial responsibility the subject will undertake must be addressed in the consent document.*

12. Vulnerable Populations:

a. Some subject groups are particularly vulnerable and require additional protections. Please check off any of the following groups that will be part of your subject population and complete the appropriate Supplement within this Application:

- [ ] Children (under age 18) (Supplement A)
- [ ] Prisoners (Supplement B)
- [ ] Pregnant Women (Supplement C)
- [ ] Cognitively Impaired (Supplement D)
- [ ] Non-English Speakers/International Research (Supplement E)

b. If you plan to enroll subjects who might be particularly vulnerable to coercion or undue influence, please provide a plan below to ensure that these subjects are not coerced or unduly influenced to participate in this research study.

*Note: Coercion is feeling forced to participate in the research or feeling that you will suffer harm if you do not. Undue influence is offering an inducement to participate in research that encourages someone to act against his/her best interest or wishes.*

c. Please provide a rational for use of special groups or subjects whose ability to give voluntary informed consent may be in question (e.g., cognitively impaired).

13. Risks:

*Note: According to HHS Regulations minimal risk means "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."*

a. If the classification is minimal risk, please justify why that category is appropriate and then skip to the Section on Benefits:

b. If the classification is greater than minimal risk, describe all of the risks (including non-physical risks) in detail and assess their seriousness.
c. What precautions have been taken to minimize these risks and what is their likely effectiveness?

d. Describe other alternative and accepted procedures to minimize risk, if any, that were considered and why they will not be used.

14. Benefits:

a. Assess the potential benefits to science and/or society which may accrue as a result of this research.

b. Are there any benefits which may accrue to the individual subjects in this research?
   □ Yes □ No If yes, please explain:

c. If the risk in this study is more than minimal, explain how the risks are reasonable in relation to the benefits:

15. Informed Consent:

Unless waived by the IRB, informed consent is necessary for all research involving human subjects and must be documented in some manner. The investigator may determine which method would best serve the interest of the subject population, but the IRB reserves the right to require alternative or more stringent means of securing consent.

a. Which of the following apply to this research:

   □ Informed consent will be obtained from all subjects and documented with a signed, written consent form. If so, answer all of the questions below.

   □ Informed consent will be obtained from subjects, but no signed consent form will be used. This includes oral consent and implied consent (e.g., completing a survey). If so, answer questions below and complete Supplement H to request a waiver of documentation of consent.

   □ Fully informed consent will not be obtained from all subjects. This includes deception, withholding information, etc. If so, complete Supplement H to request a waiver of consent and proceed to Question 16.
b. Describe the circumstances/process under which consent will be obtained, including where the process will take place and any waiting period between informing the prospective subject and obtaining consent.

c. Who will obtain consent? Describe their experience in obtaining consent from subjects.

d. How will it be determined that the subjects or the subjects' authorized representatives understand the information presented?

e. Describe the measures instituted to minimize coercion or undue influence.

f. Is the primary language of the consent process English? □ Yes □ No

If No, state the other language(s) and indicate who will provide the translation services and Certificate:

Submit the appropriately translated consent documents and Certificate of Translation provided by someone who speaks the native language and is not affiliated with the research prior to consenting Non-English speaking participants. Complete Supplement E for Non-English Speakers/International Research.

g. Does your study involve children (anyone under the age of 18)? □ Yes □ No

If Yes, child assent is required by regulation if the minor is capable of providing such assent (typically, ages 7 to 17) and complete Supplement A.

h. Will any subjects be cognitively impaired so that they may not have the capacity to give consent? □ Yes □ No

If Yes, complete Supplement D.

i. How will the subjects' informed consent be documented? Please indicate all the ways in which consent is documented:

Note: Signed, written consent forms are required unless waived by the IRB, but are not the only, or most effective forms of documentation. You must provide copies of all written consent forms.

16. Privacy & Confidentiality:
a. Explain provisions to protect privacy interests of subjects. This refers to how investigators will contact subjects and/or access private information from or about subjects during and after their involvement in the research (e.g. time, place, etc. of research procedures).

b. Will the data collected in the course of the study be considered sensitive data, e.g. mental health, HIV status, SS#, etc.? □ Yes □ No

If Yes, provide the rationale for why this data is needed:

If Yes, could any of this data, if disclosed, have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation? □ Yes □ No

If Yes, will a Certificate of Confidentiality be obtained? □ Yes □ No

c. What specific safeguards will be employed to protect confidentiality of data, e.g., coding or removal of identifiers as soon as possible, limitation of access to data, use of locked file cabinets, protection of computer-based data systems, etc.?

d. Will data that identifies individual subjects be published or in any way be disclosed to third parties other than project personnel? □ Yes □ No

If yes, please explain here and be sure to incorporate in consent form:

17. Safety Management:

For all research involving more than minimal risk, describe the safety management plan. The safety management plan should address:

- A description of the plan to monitor research progress and subject reactions, including who will do the monitoring and how monitoring will be accomplished.
- Identification of a Data Safety Monitor or Data Safety Monitoring Board, where applicable.
- A plan for dealing with adverse events and unanticipated problems involving risk to subjects or others.
- A description of the plan to assure compliance with reporting of adverse events and/or unanticipated problems involving risks to participants or others.
- A description of the plan to assure data accuracy and protocol compliance.

18. ICH-GCP (applicable only to clinical trials):

a. I certify I am conducting a clinical trial that complies with ICH- GCP requirements found in section E6. □ Yes □ No
b. If ICH-GCP applies, investigators must submit a copy of their most recent curriculum vitae or other documentation evidencing qualifications. Submitted? □ Yes □ No

If your research involves any of the following, please check which applies. Complete the appropriate supplements after the PI/Faculty Advisors Assurance Statement. The Supplements can be found at the end of this document.

Please check the box for the Supplements completed.

Children: □ Complete IRB Supplement A

Prisoners: □ Complete IRB Supplement B

Pregnant Women, Fetuses, or Neonates: □ Complete IRB Supplement C

Cognitively Impaired: □ Complete IRB Supplement D

Non-English Speakers/International Research: □ Complete IRB Supplement E

The Internet: □ Complete IRB Supplement F

Stored Data for Future Use: □ Complete IRB Supplement G

Request for Waiver of Consent and/or Documentation of Consent: □ Complete IRB Supplement H

Research Involving Physiological Processes: □ Complete IRB Supplement I

Drugs or Biologics: □ Complete IRB Supplement J

Medical Devices: □ Complete IRB Supplement K

Deception: □ Complete IRB Supplement L

Placebo: □ Complete IRB Supplement M

Conflict of Interest: □ Complete IRB Supplement N
Checklist for Biomedical Institutional Review Board Application Submission:

☐ Cover Letter - Required

☐ Application Form with electronic signature of PI and Department Head through IRBNet except for student PIs where the electronic signature of a Faculty Advisor is required in lieu of the Department Head

☐ CITI Training Certificates for all research personnel

☐ Protocol – REQUIRED - ‘Tips for Writing a Protocol’ can be found on the Tulane HRPO website at: http://tulane.edu/asypr/irb

☐ Informed Consent Documents (unless requesting a waiver of consent)
  ☐ Participant Consent Form
  ☐ Consent Information Sheet/Oral Consent Script (if requesting a Waiver)
  ☐ Parental Permission Form (if applicable)
  ☐ Child Assent Form (if applicable)

Other Materials, if applicable:

☐ Additional Supplements (A-N)
  ☐ If the research involves Stored Data for Future Use, complete Supplement G
  ☐ If the research involves Physiological Processes, complete Supplement I
  ☐ If the research involves Drugs or Biologics, complete Supplement J
  ☐ If the research involves Medical Devices, complete Supplement K
  ☐ If the research involves Deception, complete Supplement L
  ☐ If the research involves a Placebo, complete Supplement M

☐ Any and All Recruitment Materials

☐ Data Collection Instrument/Questionnaire/Survey/Investigator's Brochures/Package Inserts

☐ Approval from Sites (Foreign and Domestic)

☐ Grant and Contracts Routing Form – Must be signed by the PI and Department Head – ‘Proposal Routing Form': http://tulane.edu/asypr/ora/forms.cfm

☐ Wallet ID Card and Evacuation Contact Card

☐ $2,500 Interdepartmental Transfer Form (Industry-Sponsored Studies only)

☐ If your research involves infectious/live, attenuated, and/or pathogenic microorganisms for use in humans and/or deliberate transfer of recombinant DNA (or DNA or RNA derived from recombinant DNA) into human research participants, your protocol must be submitted to the Institutional Biosafety Committee ("IBC"): www.ibc.tulane.edu. 
  ☐ In addition, those experiments involving the deliberate transfer of recombinant DNA or RNA into humans require IBC, IRB and the NIH’s Recombinant DNA Advisory Committee ("RAC") approvals before research participant enrollment
Translated Documents and Certificate Verifying Translation

Curriculum vitae if ICH-GCP applies

**Checklist for Social/Behavioral Institutional Review Board Application Submission:**

- Cover Letter - Required
- Application Form with electronic signature of PI and Department Head through IRBNet except for student PIs where the electronic signature of a Faculty Advisor is required in lieu of the Department Head
- CITI Training Certificates for all research personnel
- Protocol – REQUIRED - ‘Tips for Writing a Protocol’ can be found on the Tulane HRPO website at: http://tulane.edu/asvpr/irb
- Informed Consent Documents (unless requesting a waiver of consent)
  - Participant Consent Form
  - Consent Information Sheet/Oral Consent Script (if requesting a Waiver)
  - Parental Permission Form (if applicable)
  - Child Assent Form (if applicable)

Other Materials, if applicable:

- Additional Supplements (A-N)
  - If the research involves Stored Data for Future Use, complete Supplement G
  - If the research involves Physiological Processes, complete Supplement I
  - If the research involves Deception, complete Supplement L
  - If the research involves a Placebo, complete Supplement M
- Any and All Recruitment Materials
- Data Collection Instruments/Questionnaires/Surveys/Interview Questions/Focus Group Guide
- Approval from Study Sites (Foreign and Domestic)

- Grant and Contracts Routing Form – Must be signed by the PI and Department Head - ‘Proposal Routing Form’: http://tulane.edu/asvpr/ora/forms.cfm
- Debriefing Plan if study involves Deception
- Translated Documents
- Certificate Verifying Translations
Principal Investigator Assurance Statement:

I certify that the information provided in this application is complete and correct.

I understand that as Principal Investigator, I have the responsibility for the conduct of the study, the ethical performance of the project and protection of the rights and welfare of human participants.

I agree to comply and assure that all affiliated personnel comply with all Tulane HRPO policies and procedures, as well as with all applicable federal, state, and local laws regarding the protection of human participants in research.

I assure that this study is performed by qualified personnel adhering to the Tulane IRB approved protocol.

I assure that no modification to the approved protocol and consent materials will be made without first submitting for review and approval by the Tulane IRB an amendment to the approved protocol.

I agree to obtain legally effective informed consent from the research participants as applicable to this research and as prescribed in the approved protocol.

I will promptly report unanticipated problems to the Tulane IRB by using the appropriate form.

I will adhere to all requirements for continuing review.

I will advise the Tulane IRB of any change of address or contact information as long as this protocol remains active.

I assure that I have obtained all necessary approvals from entities other than Tulane IRB that are necessary to conduct this research.

By my electronic signature on this study/package, I certify that I am knowledgeable about the regulations and policies governing research with human subjects and have sufficient training and experience to conduct this particular study in accordance with the research protocol.

Department Head/Dean Assurance Statement:

By my electronic signature on this study/package, I certify that this protocol has been reviewed and approved for submission to the Institutional Review Board for Human Research. I have reviewed the project and believe that the benefits outweigh the potential risks. I consider it a suitable research project for my Department. If I become aware of any information regarding the suitability of this research project, I will immediately notify the IRB Committee Chairman.

Note: If the Principal Investigator is a Department Head, then the signature of the Dean of the school is required.
If the PI is a student and a Faculty Advisor is appointed, the faculty advisor must electronically sign the package/study through IRBNet.

Faculty Advisor's Assurance

By my electronic signature as a Faculty Advisor on this research application, I certify that the student is knowledgeable about the regulations and policies governing research with human subjects and has sufficient training and experience to conduct this particular study in accordance with the research protocol. Additionally:

I hereby confirm that I have thoroughly reviewed this IRB application, including the protocol narrative, and verify that it is complete and the research is appropriate in design.

I agree to meet with the investigator on a regular basis to monitor study progress.

I assure that the investigator will promptly report unanticipated problems to the IRB and will adhere to all requirements for continuing review.

If I will be unavailable (e.g. sabbatical leave, vacation or resignation), I will arrange for an alternate faculty sponsor to assume responsibility during my absence, and I will advise the Tulane IRB, in writing, of such changes.

If the student leaves the university, I will provide all the necessary documents for terminating the study or continuing review.
Tulane University Institutional Review Board
Application for Continuing Review

The Department of Health and Human Services regulations for the protection of human subjects at 45 CFR 46.109(e) require that all non-exempt studies approved by IRBs undergo a Continuing Review at least once a year.

Some studies may require more frequent review depending on their level of risk. During the Continuing Review process, the entire study is examined to determine whether the anticipated risks and benefits have changes and whether the safeguards put in place at the time of prior approval remain adequate for the protection of human research participants.

Federal regulations require that a study must be terminated if it does not undergo review before the approval period expires. Federal regulations do not permit a grace period. It is the investigator's responsibility to apply for continuing review in a timely manner. If a Continuing Review Application is not submitted prior to the date of expiration, a new application for Tulane University IRB approval must be submitted, reviewed, and approved before the research can be resumed.
Protocol Title:
Tulane University IRB #:
Date of Expiration:

Section A: General Information

1. Principal Investigator:

<table>
<thead>
<tr>
<th>Name:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Email:</td>
</tr>
</tbody>
</table>

Section B: Current Status of Research

2. Specify the Study’s Current Status Below – Note: if all research-related activities have been completed, the study has been terminated, or the study was never initiated, use the “Study Closure Form.”

☐ Enrollment has not yet begun
☐ Enrollment is in progress
☐ Closed to enrollment but contact with the participants is ongoing (any interventions, treatments)
☐ Closed to enrollment but follow-up of subjects continues
☐ Closed to enrollment but data analysis continues

Comments:

Section C: Study History

3. Funding Status – Note: Submit the grant proposal or contract if not on file with the IRB

☐ Project is currently funded:
   Funding Agency (e.g. NIH):
   Grant/Contract Number:

☐ No Funding Obtained or Applied For.

☐ Project has been submitted for funding:
   Funding Agency (e.g. NIH):

☐ Industry-Sponsored

4. Please briefly describe the research protocol.
5. How many participants have been approved by the Tulane University IRB (locally)?

6. How many participants have been enrolled since the start of the study?

7. How many participants have been enrolled since the last IRB Review and Approval Date?

8. Have any participants withdrawn or been removed from this study? If Yes, please explain.

9. Have any unanticipated problems, adverse events (expected and unexpected), or complications occurred since the last date of IRB approval? If Yes, please explain.

10. Have you received any complaints from participants about the research since the last date of IRB approval? If Yes, please explain.

11. Since the last IRB approval date, has any new information become available that would alter the project's risk/benefit ratio (e.g. any relevant recent literature; any interim findings, including data safety monitoring reports, any relevant multi-center trial reports.) If Yes, please explain.

12. Has the IRB approved the participation of vulnerable populations for this study? If Yes, please provide the cumulative accrual of each vulnerable population:

<table>
<thead>
<tr>
<th>Category</th>
<th>Total Enrolled:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Students/Employees of Tulane University</td>
<td></td>
</tr>
<tr>
<td>Pregnant Women</td>
<td></td>
</tr>
<tr>
<td>Children</td>
<td></td>
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<tr>
<td>Prisoners</td>
<td></td>
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<tr>
<td>Persons with Cognitive, Social, or Economic, or Educational Disadvantages</td>
<td></td>
</tr>
<tr>
<td>Non-English Speaking Persons</td>
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</tbody>
</table>

Issued: 9/24/09
Effective: 1/6/10
Form #: 603

Last Reviewed: 1/6/10
Last Revised: 1/6/10
13. Have any subjects been excluded on the basis of race, ethnic group, understanding of English, socioeconomic status, education, gender, or pregnancy? If Yes, please explain.

14. What is the gender and minority status of those entered into the protocol?

Section D: Update on Research Risks/Benefits

15. Since the last IRB review, have subjects experienced any additional benefits from the research? If Yes, please explain.

16. In the opinion of the Principal Investigator, have the risks or potential benefits of this research changed? If Yes, please explain.

Section E: Changes in Research

*Note: All Modifications and/or Changes that have not been reviewed and approved by the IRB must be submitted. Changes may not be implemented without prior IRB approval.*

17. Since the last IRB review, have there been any problems with or any changes to the research (including the following: subject recruiting, advertising, subject compensation, inclusion or exclusion criteria, costs to subjects, consent process, documentation of informed consent, privacy or confidentiality, safety monitoring, subject populations, etc.)? If Yes, please provide a summary of the problems/changes.

*Note: If the protocol has changed in any way since the last IRB review, an Updated Protocol must be submitted with the Application.*

Section F: The Consent Process

Types of Informed Consent Approved by the IRB:

- Written Informed Consent Document(s)
- Oral Script/Information Sheet/or Waiver of Documentation of Informed Consent
- Waiver of Informed Consent

If you are enrolling participants, an updated Consent Form(s) and/or Assent Form with an updated Version Date in the footer of the document must be included with this application in order to be approved for the renewal period.

If you are requesting approval of new consent documents or changes to previously approved consent documents, indicate this below. New consent documents and changes cannot be implemented without prior IRB approval. If you have enrolled subjects since the last approval period, you must submit the last two signed Consent Forms with signatures and initials blacked out.

18. Did you submit a Waiver of Consent request previously? □ Yes □ No

19. Are you enrolling subjects and therefore submitting updated Consent/Assent documents?

20. Are you requesting changes to previously approved consent documents? If Yes, please describe the changes below and submit two versions of each consent form for which you are requesting changes: one version highlighting the changes and the other version with the changes finalized.

Section G: Summary of Progress

21. Please provide a brief summary of the research progress to date. State if there are no findings available at the present time.

22. Please list any other information specific to this study that you believe the IRB should consider.

Section H: Attachments

23. Please attach the following items as applicable and check the boxes for the documents attached for review:

□ Cover Letter - Required
□ CITI Training Certificates for all research personnel
□ Updated/New/Revised Protocol
□ Updated/New/Revised Consent Form
□ Updated/New/Revised Assent Form
If you have enrolled subjects since the last approval period, you must submit the last two signed Consent Forms with the signatures blocked out.

- Translated Versions of Updated/Revised/New Consent Documents with certificate verifying translation
- DSMB Report
- Federal Grant/Contract Application
- IT (Industry-Sponsored Project) for $1000
- Investigator's Brochure
- Sponsor Progress Report
- Other:

**Section I: ICH-GCP**

24. The ICH-GCP requirements apply to all clinical trials. If so, as the investigator, I certify that the clinical trials complies with the ICH-GCP requirements found in section E6. □ Yes □ No

**Section J: Principal Investigator’s Statement of Assurance**

I certify that the information provided in this application is complete and correct.

I understand that I cannot initiate any changes in my approved protocol before I have received IRB approval and/or complied with all contingencies/stipulations with regards to that approval. By electronically signing this form, I certify that all relevant information concerning unanticipated problems or other issues that might affect the risk/benefit ratio of this study has been disclosed to the IRB.

Also, I certify that all of the appropriate documents will be submitted to the IRB for review including a study closure form if the research is completed over the course of the approval period.

25. If there has been a lapse in IRB Approval, what research-related activities have occurred during the period for which there was no IRB approval?
Tulane
Interdepartmental Order Form

ID#: 561785

Effective Date: [X] [X] [X] [X]
Expenditure Date: [X] [X] [X] [X]

Category: Interdepartmental Order
Prepared By: John Horne

Approved By (Accounting Use Only):

<table>
<thead>
<tr>
<th>General Ledger Journal</th>
<th>IRB Initial or CR</th>
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<td>[X] [X] [X] [X]</td>
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<tr>
<th>Grants Management Journal</th>
<th>Statement of Award</th>
<th>Expenditure Description</th>
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**INITIAL SUBMISSION FEE OR CONTINUING REVIEW FEE**

**STUDY TITLE, STUDY NUMBER, PI NAME**

<table>
<thead>
<tr>
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<tbody>
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<th>Date</th>
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<th>Service or Material Delivered</th>
<th>Date</th>
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Authorized Signature: [X] Date

Authorized Signature: [X] Date
TULANE UNIVERSITY HRPO:

IRBNet USERS GUIDE

(Revised: August 2010)

Effective October 16, 2009, the Tulane University Human Research Protecions Office adopted the IRBNet Internet-based submission system. The HRPO will only accept submissions electronically through IRBNet. This Users Guide provides step-by step instructions for each type of submission.

The Web Address:

www.irbnet.org

If you have any questions regarding submitting via IRBNet, please contact the HRPO at 504-988-2665 or email us at irbmain@tulane.edu.

Thank You!
TABLE OF CONTENTS:

REGISTERING WITH IRBNET ................................................................. PAGE 2
INITIAL SUBMISSIONS ................................................................. PAGE 3
CONTINUING REVIEWS ................................................................ PAGE 6
AMENDMENTS ................................................................................ PAGE 8
STUDY CLOSURES ........................................................................ PAGE 10
UNANTICIPATED PROBLEMS/PROTOCOL DEVIATIONS .................. PAGE 12
RESPONSES TO DEFERALS/ INFORMATION REQUIRED LETTERS .... PAGE 14
RESPONSES TO UNLOCKED SUBMISSIONS .................................... PAGE 15
OTHER SUBMISSIONS ...................................................................... PAGE 16
LOCATING DECISION LETTERS ..................................................... PAGE 17
SUBMISSION TYPE GUIDELINES .................................................. PAGE 18
INSTRUCTIONS FOR REGISTERING WITH IRBNET:

1. Go to http://www.irbnet.org

2. Click on the ‘New User Registration’ link in the upper right-hand corner of the screen

3. Create your username and password. Fill out the required information. Your password must contain 8 characters. Click ‘Continue’

   Note: This system does not interface with Tulane University’s system, but you may choose to use your Tulane University username and password if you would like.

4. Read and accept the Individual User Terms of Use

5. To add your affiliation, type the word ‘Tulane’ into the search box. UNCHECK ‘Boards’ and ‘Sponsors’ leaving only ‘Research Institutions’ checked. Click ‘Display’. Select ‘Tulane University’ from the organization box. Click ‘Continue’

6. Enter your contact information. Enter the email address you would like to receive communications through the IRBNet system. (e.g. notification of IRB decisions, communications from your research team or administrator). Click ‘Continue’

7. Review your provided information and edit as necessary. When you are satisfied, click ‘Register’

An email will be sent to the email address you provided in Step 6, with ‘IRBNet Activation Required’ in the subject line. You will need to click on the link provided in this registration email in order to activate your account.

Clicking on the link will take you to the IRBNet homepage.
INSTRUCTIONS FOR INITIAL SUBMISSIONS:

Note: An instructional video is available on our website for submitting new submissions via IRBNet, please go to http://tulane.edu/asvpr/irb and click on the video.

*IF YOU HAVE AN OPEN STUDY (BEFORE OCTOBER 2009), CONTACT THE HRPO AT irbmain@tulane.edu AND THE STUDY WILL BE TRANSFERRED TO YOU AND YOU MAY ADD PACKAGES (SUBMISSIONS) TO THE PROJECT. DO NOT CREATE A NEW PROJECT.

IF YOU ARE CREATING A NEW PROJECT, FOLLOW THESE INSTRUCTIONS:

Step 1: Log in to www.irbnet.org using your username and password (for First Time Users, you must Register with IRBNet; please see INSTRUCTIONS FOR REGISTERING WITH IRBNET WITHIN THIS GUIDE).

Step 2: The default page will be MY PROJECTS, where you will have access to all of your studies and create new studies.

Click CREATE NEW PROJECT, fill in the relevant information about your project, and click ‘Continue’

Step 3: You will now be on the DESIGNER page where you will download forms, templates, and reference materials to assemble a new study.

NOTE: INITIAL APPLICATION PART 1 (THE ON-LINE DOCUMENT) MUST BE COMPLETED FIRST FOR ALL INITIAL SUBMISSIONS.

A. To locate it, Select ‘Tulane University’ from the ‘Select a Library’ drop-down menu, then click ‘ADD NEW DOCUMENT’

B. Go to the on-line document section at the bottom and click ‘ADD’ and then ‘NEXT’ to navigate the form. Complete this form then click ‘SAVE AND EXIT’. A PDF will be created and the completed form will be added to the designer.

In the ‘Select a Document’ drop-down menu, you will find all of the IRB Forms, Checklists, etc. If you have questions about what is needed for submitting a complete project, you may download the ‘Initial Submission Checklist’ which lists everything required for an Initial Submission.
All required forms are to be downloaded to your computer, completed and saved to your computer, and attached to the submission.

To attach documents, Click ‘ADD NEW DOCUMENT’, select the document type, add description of document (the document description should be the document title as listed on your cover letter), click ‘ATTACH’.

Step 4: SHARE THIS PROJECT with your research team. Click the ‘Share this Project’ button; click the blue ‘Share’ link to grant access to this project.

Select ‘Tulane University’ from the organization box; click ‘Select Organization’ and search for registered users with whom you’d like to share this project (i.e. your Faculty Advisor, Co-Investigators, Research Assistants, Department Head, Dean, etc.) Grant each user a level of access:

FULL: User may add/edit/delete project documents, share the project with other users, and submit the project. Individuals with full access to a project will receive auto-notification when an action has been taken regarding the project.

It is recommended that students give this level of access to their Faculty Advisors.

WRITE: User may add/delete project documents, but cannot share the project with other users or submit the project

READ: User may only view project documents

NOTE: TO ‘SHARE’ YOUR PROJECT WITH SOMEONE, THEY MUST BE REGISTERED WITH IRBNET.ORG.

Selected users will be notified automatically via email that the project has been shared with them, you may enter comments to be included within the email.

Step 5: Click SIGN THIS PACKAGE. The PI and The Department Head must sign the project before it is submitted. If the PI is the Department Head, then the Dean of School must sign the project before it is submitted. If the PI is a student, the PI and the Faculty Advisor must sign the project before it is submitted. Select your role and click ‘Sign’

The lead researcher should sign as “Principal Investigator” A designee may NOT sign for the PI.

The project will need to be ‘SHARED’ will all signatories so that they may have access to the project to sign it.

The Faculty Advisor should sign as the “Advisor”

The Department Head should sign as the “Department Head”

Note: Studies will not be scheduled for review if required signatures are missing.
Step 6: Click SUBMIT THIS PACKAGE. Select “Tulane University” in the “Search for Organization” drop down menu (This will be your default location and should be highlighted already). Click either “Tulane University Biomedical IRB” for Biomedical Submissions or click “Tulane University Social-Behavioral IRB” for Social-Behavioral Submissions. Then click the ‘Continue’ button. In the Submission Type drop-down menu, select ‘New Project’ and click ‘Submit’

Be sure all documents are attached and in the final version prior to submitting.

Once a decision letter is formulated, an automatic email will be sent to everyone who has full access and the letter and any supporting documents can be printed.

**TIPS:**

- When submissions are incomplete you will receive an email that will list what is missing. Please follow the instructions in that email to complete your submission.
- The MY PROJECTS screen can be found by clicking on ‘My Projects.’ This will show you the list of studies to which you have access.
- Projects which have NOT been submitted to the IRB are labeled “Work in Progress” in the Status column.
- Studies which have been submitted to the IRB but not reviewed by the IRB are labeled “Pending Review.”
- Clicking on the title of any project will take you to the PROJECT OVERVIEW for the selected project which contains project details. This page will show the project status.
- An automatic email message will be sent to everyone with full access to the project when someone has signed the submission. You can also check by clicking sign this package.
- To Un-Share a project with someone, follow the same steps in SHARE THIS PROJECT and click on “No Access.”
INSTRUCTIONS FOR SUBMITTING A CONTINUING REVIEW:

THE SUBMISSION OF A CONTINUING REVIEW OF AN OPEN STUDY REQUIRES THE CREATION OF A SUBSEQUENT PACKAGE IN A PROJECT.

*IF YOU ARE SUBMITTING A CONTINUING REVIEW FOR A STUDY OPENED BEFORE OCTOBER 2009, CONTACT EITHER THE PI TO GIVE YOU ACCESS, OR THE HRPO AT irbmain@tulane.edu AND THE STUDY WILL BE TRANSFERRED TO YOU AND YOU MAY ADD PACKAGES (SUBMISSIONS) TO THE PROJECT. DO NOT CREATE A NEW PROJECT.

Step 1: Login to IRBNet; www.irbnet.org. This will take you to the MY PROJECTS page. This is where all of the studies that you have access to will be housed.

Step 2: Click on the Title of the project that you would like to continue/renew. If the project is not listed on your my projects page then you should contact the PI to give you access. Then click on the PROJECT HISTORY

Step 3: Click on the CREATE NEW PACKAGE button and then NEW DOCUMENT PACKAGE

Step 4: You will now be on the DESIGNER page.

NOTE: IF INITIAL APPLICATION PART 1 HAS NOT PREVIOUSLY BEEN COMPLETED FOR THIS STUDY ON IRBNET, FOLLOW THE STEPS BELOW:

A. To locate it, Select ‘Tulane University’ from the ‘Select a Library’ drop-down menu, then click ‘ADD NEW DOCUMENT’
B. Go to the on-line document section at the bottom and click ‘ADD’ and then ‘NEXT’ to navigate the form. Complete this form then click ‘SAVE AND EXIT’. A PDF will be created and the completed form will be added to the designer.

Select your library (the IRB in which you originally submitted this study’s documents, Tulane University Biomedical or Social-Behavioral IRB). Next, select the ‘Secondary Submission Checklist’ from the ‘Select a Document’ drop-down menu, and click ‘Download’. From here you can determine what documents are required for a complete continuing review. All required forms are to be downloaded to your computer, completed and saved to your computer, and attached to the submission.

To attach documents, Click ‘ADD NEW DOCUMENT’, select the document type, add description of document (the document description should be the document title as listed on your cover letter), click ‘ATTACH’.
Step 5: If adding /changing any Co-investigators, Coordinators, etc., share the project with your research team by clicking SHARE THIS PROJECT Click the blue ‘Share’ link within the text to grant access to this project.

Select Tulane University from the organization box, click ‘Continue’

NOTE: TO ‘SHARE’ YOUR PROJECT WITH SOMEONE, THEY MUST BE REGISTERED WITH IRBNET.ORG.

Grant each user a level of access: FULL, WRITE, or READ

Selected users will be notified automatically via email that the project has been shared with them. You may enter comments to be included in this email in the ‘Your Comments’ section. Click ‘Save’

Step 6: Click SIGN THIS PACKAGE. (Only PIs are required to sign the submission.)

Select your role and click ‘Sign’

The lead researcher should sign as “Principal Investigator” A designee may NOT sign for the PI.

Studies will not be scheduled for review if required signatures are missing.

Step 7: Once you have attached all of your documents and project is signed, you should be ready to submit your project. Click on SUBMIT THIS PACKAGE; click on “Tulane University Biomedical IRB” for Biomedical Submissions and click on “Tulane University Social-Behavioral IRB” for Social-Behavioral Submissions in the ‘Select Organization’ box.

Then click on the ‘Continue’ button. In the Submission Type drop-down menu, select ‘Continuing Review/Progress Report’ and click ‘Submit’

To confirm that your submission has been submitted, click PROJECT OVERVIEW. The submission status will be ‘Pending Review’ until a decision has been made.
INSTRUCTIONS FOR SUBMITTING AN AMENDMENT:

THE SUBMISSION OF AN AMENDMENT OF AN OPEN STUDY REQUIRES THE CREATION OF A SUBSEQUENT PACKAGE IN A PROJECT.

*IF YOU ARE SUBMITTING AN AMENDMENT FOR A STUDY OPENED BEFORE OCTOBER 2009, CONTACT EITHER THE PI TO GIVE YOU ACCESS, OR THE HRPO AT irbmain@tulane.edu AND THE STUDY WILL BE TRANSFERRED TO YOU AND YOU MAY ADD PACKAGES (SUBMISSIONS) TO THE PROJECT. DO NOT CREATE A NEW PROJECT.

Step 1: Login to IRBNet; www.irbnet.org. This will take you to the MY PROJECTS page.

Step 2: Click on the Title of the project that you would like to amend/modify. Then click on the PROJECT HISTORY.

Step 3: Click on the CREATE NEW PACKAGE button and then the NEW DOCUMENT PACKAGE.

Step 4: You will now be on the DESIGNER page.

NOTE: IF INITIAL APPLICATION PART 1 HAS NOT PREVIOUSLY BEEN COMPLETED FOR THIS STUDY ON IRBNET, FOLLOW THE STEPS BELOW:

A. To locate it, Select ‘Tulane University’ from the ‘Select a Library’ drop-down menu, then click ‘ADD NEW DOCUMENT’

B. Go to the on-line document section at the bottom and click ‘ADD’ and then ‘NEXT’ to navigate the form. Complete this form then click ‘SAVE AND EXIT’. A PDF will be created and the completed form will be added to the designer.

Select your library (the IRB in which you originally submitted this study’s documents, Tulane University Biomedical or Social-Behavioral IRB). Next, select the ‘Secondary Submission Checklist’ from the ‘Select a Document’ drop-down menu, and click ‘Download’. From here you can determine what documents are required for a complete amendment submission. All required forms are to be downloaded to your computer, completed and saved to your computer, and attached to the submission.

To attach documents, Click ‘ADD NEW DOCUMENT’, select the document type, add description of document (the document description should be the document title as listed on your cover letter), click ‘ATTACH’.

Upload any additional documents/materials for review by continuing to attach the documents to the submission.
Once all documents are attached, continue

Step 5: If adding /changing any Co-investigators, Coordinators, etc., share the project with your research team by clicking SHARE THIS PROJECT Click the blue ‘Share’ link within the text to grant access to this project.

Select Tulane University from the organization box, click ‘Continue’

NOTE: TO ‘SHARE’ YOUR PROJECT WITH SOMEONE, THEY MUST BE REGISTERED WITH IRBNET.ORG.

Grant each user a level of access: FULL, WRITE, or READ

Selected users will be notified automatically via email that the project has been shared with them. You may enter comments to be included in this email in the ‘Your Comments’ section. Click ‘Save’

Step 6: Click SIGN THIS PACKAGE. Only the PI signature is required for Modifications (if needed, the Amendment creator will need to share with the PI.)

The lead researcher should sign as “Principal Investigator” A designee may NOT sign for the PI. Studies will not be scheduled for review if the PI has not signed off on the Amendment.

Step 7: Click on SUBMIT THIS PACKAGE; click on “Tulane University Biomedical IRB” for Biomedical Submissions and click on “Tulane University Social-Behavioral IRB” for Social-Behavioral Submissions in the ‘Select Organization’ box.

Then click on the ‘Continue’ button.

In the Submission Type drop-down menu, select ‘Amendment/Modification’ and click ‘Submit’

To confirm that your submission has been submitted, click PROJECT OVERVIEW. The submission status will be ‘Pending Review’ until a decision has been made.
INSTRUCTIONS FOR SUBMITTING A STUDY CLOSURE:

THE SUBMISSION OF A STUDY CLOSURE OF AN OPEN STUDY REQUIRES THE CREATION OF A SUBSEQUENT PACKAGE IN A PROJECT.

*IF YOU ARE SUBMITTING A STUDY CLOSURE FOR A STUDY OPENED BEFORE OCTOBER 2009, CONTACT EITHER THE PI TO GIVE YOU ACCESS, OR THE HRPO AT irbmain@tulane.edu AND THE STUDY WILL BE TRANSFERRED TO YOU AND YOU MAY ADD PACKAGES (SUBMISSIONS) TO THE PROJECT. DO NOT CREATE A NEW PROJECT.

Step 1: Login to IRBNet; www.irbnet.org. This will take you to the MY PROJECTS page.

Step 2: Click on the Title of the project that you would like to close. Then click on the PROJECT HISTORY

Step 3: Click on the CREATE NEW PACKAGE button and then the NEW DOCUMENT PACKAGE

Step 4: You will now be on the DESIGNER page.

Select your library (the IRB in which you originally submitted this study's documents, Tulane University Biomedical or Social-Behavioral IRB). Next, select the 'Secondary Submission Checklist' from the 'Select a Document' drop-down menu, and click 'Download'. From here you can determine what documents are required for a complete study closure submission. All required forms are to be downloaded to your computer, completed and saved to your computer, and attached to the submission.

To attach documents, Click 'ADD NEW DOCUMENT', select the document type, add description of document (the document description should be the document title as listed on your cover letter), click 'ATTACH'.

Upload any additional documents/materials for review by continuing to attach the documents to the submission.

Once all documents are attached, continue

Step 5: Click SIGN THIS PACKAGE. Only the PI signature is required for Study Closures (if needed, the Study Closure submission creator will need to share with the PI.)

The lead researcher should sign as “Principal Investigator” A designee may NOT sign for the PI. Studies will not be scheduled for review if the PI has not signed off on the Closure.
Step 6: Click on SUBMIT THIS PACKAGE; click on “Tulane University Biomedical IRB” for Biomedical Submissions and click on “Tulane University Social-Behavioral IRB” for Social-Behavioral Submissions in the ‘Select Organization’ box. Then click on the ‘Continue’ button.

In the Submission Type drop-down menu, select ‘Closure/Final Report’ and click ‘Submit’

To confirm that your submission has been submitted, click PROJECT OVERVIEW. The submission status will be ‘Pending Review’ until a decision has been made.
INSTRUCTIONS FOR SUBMITTING UNANTICIPATED PROBLEMS/PROTOCOL DEVIATIONS/VIOLATIONS/OTHER REPORTABLE EVENTS

THE SUBMISSION WILL REQUIRE THE CREATION OF A SUBSEQUENT PACKAGE IN A PROJECT.

*IF YOU ARE SUBMITTING FOR A STUDY OPENED BEFORE OCTOBER 2009, CONTACT EITHER THE PI TO GIVE YOU ACCESS, OR THE HRPO AT irbmain@tulane.edu AND THE STUDY WILL BE TRANSFERRED TO YOU AND YOU MAY ADD PACKAGES (SUBMISSIONS) TO THE PROJECT. DO NOT CREATE A NEW PROJECT.

If you are unsure whether to submit as an Adverse Event or a Reportable Event, consult the HRPO website for guidance or email the HRPO at irbmain@tulane.edu.

Step 1: Login to IRBNet; www.irbnet.org. This will take you to the MY PROJECTS page.

Step 2: Click on the Title of the project of which you are reporting. Then click on the PROJECT HISTORY.

Step 3: Click on the CREATE NEW PACKAGE button and then the NEW DOCUMENT PACKAGE.

Step 4: Click the DESIGNER.

If submitting a Reportable Event, select the appropriate library and here you will find the Unanticipated Problems Report Form and the Protocol Deviation, Violation & Exception Reporting Form. Fill out the appropriate form/s and upload them to the submission along with any other additional materials such as sponsor reports, etc as stated on the Secondary submission checklist.

Step 5: Click SIGN THIS PACKAGE. Only the PI signature is required for these reports (if needed, the submission creator will need to share with the PI.)

The lead researcher should sign as “Principal Investigator” A designee may NOT sign for the PI. Studies will not be scheduled for review if the PI has not signed off on the submission.

Step 6: Click on SUBMIT THIS PACKAGE; click on “Tulane University Biomedical IRB” for Biomedical Submissions and click on “Tulane University Social-Behavioral IRB” for Social-Behavioral Submissions in the ‘Select Organization’ box.

Then click on the ‘Continue’ button.

In the Submission Type drop-down menu, select the appropriate submission type, either ‘Adverse Event’ or ‘Reportable Event (Non-AE)’ and click ‘Submit’
To confirm that your submission has been submitted, click PROJECT OVERVIEW. The submission status will be 'Pending Review' until a decision has been made.
INSTRUCTIONS FOR SUBMITTING RESPONSES TO DEFERRALS/INFORMATION REQUIRED LETTERS

THE SUBMISSION WILL REQUIRE THE CREATION OF A SUBSEQUENT PACKAGE WITHIN THE PROJECT, DO NOT CREATE A NEW PROJECT.

Step 1: Login to IRBNet; www.irbnet.org. This will take you to the MY PROJECTS page.

Step 2: Click on the Title of the project of which you submitting revisions. Then click on the PROJECT HISTORY

Step 3: Click on the CREATE NEW PACKAGE button and then the NEW DOCUMENT PACKAGE

Step 4: Click the DESIGNER.

From here, you can upload revised documents for your study by clicking on ‘Add New Document’. Browse for your revised documents and any other relevant information from your computer and assign the proper Document Type from the drop down menu. Click ‘Attach’.

Note: You must submit a Memo (or Cover Letter) with a point-by-point response to each of the items addressed in the deferral letter; and, if applicable, revised study documents. Please include tracked and clean copies of revised documents.

Step 5: Click SIGN THIS PACKAGE. The PI signature is required for these revisions (if needed, the submission creator will need to share with the PI.)

The lead researcher should sign as “Principal Investigator” A designee may NOT sign for the PI. Studies will not be scheduled for review if the PI has not signed off on the Closure.

Step 6: Click on SUBMIT THIS PACKAGE; click on “Tulane University Biomedical IRB” for Biomedical Submissions and click on “Tulane University Social-Behavioral IRB” for Social-Behavioral Submissions in the ‘Select Organization’ box.

Then click on the ‘Continue’ button.

In the Submission Type drop-down menu, select ‘Revisions’ and click ‘Submit’

To confirm that your submission has been submitted, click PROJECT OVERVIEW. The submission status will be ‘Pending Review’ until a decision has been made.
INSTRUCTIONS FOR SUBMITTING RESPONSES TO UNLOCKED SUBMISSIONS OR REVISIONS REQUESTED BY THE HRPO

You will receive an email that lists what is missing or what changes need to be made to your submission.

Step 1: Login to IRBNet; www.irbnet.org. This will take you to the MY PROJECTS page.

Step 2: Click on the Title of the project of which you submitting missing/corrected documents.

Step 3: Click the DESIGNER or you may have to go to PROJECT HISTORY to access the appropriate package.

Click on VIEW HISTORY in the designer to view the email that lists what is missing or what changes need to be made to your submission.

From here, you can upload revised documents for your study by clicking on ‘Add New Document’. Browse for your revised documents and any other relevant information from your computer and assign the proper Document Type from the drop down menu. Click ‘Attach’.

Step 4: Relock the package: Go back to the DESIGNER. Click on ‘Mark Revisions Complete’ in the upper right hand corner of the Designer page.

DO NOT CLICK SUBMIT THIS PACKAGE! The IRB already has your submission so you do not need to re-submit.
INSTRUCTIONS FOR SUBMITTING OTHER SUBMISSIONS

(such as: Other Correspondences or Communications from Study Sponsor)

An investigator is responsible for reporting any new information as it is obtained during the study.

Other submissions besides the submission types listed above are submitted using the same methods.

Step 1: Log-In to www.irbnet.org

Step 2: Click the appropriate title of the study

Step 3: Access the Designer by clicking on the PROJECT HISTORY

Step 4: Click on the CREATE NEW PACKAGE button and then the NEW DOCUMENT PACKAGE

You will now be on the DESiGNER page.

Click the 'Add New Document' icon

Attach the Document(s)

Step 5: Have the PI Sign the Package

Step 6: Submit the package to the appropriate IRB (Tulane University Biomedical or Social-Behavioral) by designating the 'Other' Submission Type.
INSTRUCTIONS FOR LOCATING YOUR ACTION/DECISION LETTER

Step 1: Login to IRBNet; www.irbnet.org. This will take you to the MY PROJECTS page.

Step 2: Click on the Title of the project for which you would like to retrieve the action letter.

Step 3: Click on PROJECT HISTORY and then the PACKAGE TYPE of the specific submission (package #).

Step 4: Click on PROJECT OVERVIEW and then REVIEW DETAILS. The action letter is located in the BOARD DOCUMENTS section at the bottom of the page.
When submitting the following items, use the appropriate SUBMISSION TYPE within IRBNet:

<table>
<thead>
<tr>
<th>ITEM:</th>
<th>SUBMISSION TYPE:</th>
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<tr>
<td>Exempt Initial Submission</td>
<td>New Project</td>
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<tr>
<td>Expedited/Convened IRB Initial Submission</td>
<td>New Project</td>
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<tr>
<td>ITs/Grants and Contracts Routing Form</td>
<td>Funding/Grant</td>
</tr>
<tr>
<td>Continuing Review</td>
<td>Continuing Review/Progress Report</td>
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<tr>
<td>Amendment</td>
<td>Amendment/Modification</td>
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<tr>
<td>Consent Revision</td>
<td>Amendment/Modification</td>
</tr>
<tr>
<td>Protocol Revision</td>
<td>Amendment/Modification</td>
</tr>
<tr>
<td>Study Closure</td>
<td>Closure/Final Report</td>
</tr>
<tr>
<td>Response to Deferral/Information Required Letter</td>
<td>Response/Follow-Up</td>
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<tr>
<td>Correspondence</td>
<td>Other</td>
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<tr>
<td>Any Communications from Sponsor</td>
<td>Other</td>
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<tr>
<td>(DSMBs, Investigator Brochures, Clarification Memos, Package Inserts) NOT REQUIRING AN AMENDMENT/MODIFICATION</td>
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<tr>
<td>External SAEs from Sponsor</td>
<td>Adverse Event</td>
</tr>
<tr>
<td>Local SAEs</td>
<td>Reportable Event/ (Non AE)</td>
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<tr>
<td>Protocol Deviation</td>
<td>Reportable Event/ (Non AE)</td>
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<tr>
<td>Unanticipated Problem</td>
<td>Reportable Event/ (Non AE)</td>
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<tr>
<td>Compliance Concern</td>
<td>Reportable Event/ (Non AE)</td>
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Please Note: CIRB submissions and MOAs follow the same instructions within this Users Guide
Section 8 of the Tulane University HRPO SOPs:

Unanticipated Problems Involving Risks to Subjects or Others

8.1 Policy
Tulane complies with DHHS and FDA regulations which state that institutions must have written policies on reporting Unanticipated Problems Involving Risks to Subjects or Others (as defined below) to the IRB, institutional officials and relevant Federal agencies and departments. The following procedures describe how Unanticipated Problems Involving Risk to Subjects or Others are handled in Research under the auspices of HRPO. Refer to HRPO’s Website for the Decision Tree for Reporting Unanticipated Problems to IRB to facilitate determining whether a reportable Unanticipated Problem exists.

8.2 Definitions
"Adverse Event" (or "AE") is any untoward physical or psychological occurrence in a Human Subject participating in Research, including any abnormal sign (e.g., abnormal physical exam or laboratory finding, symptoms or disease associated with the Research or the use of a medical investigational Test Article), symptom, or disease, temporarily associated with the Subject’s participation in the Research. An AE does not necessarily have to have a causal relationship with the Research, or any risk associated with the Research or the Research intervention, or the assessment.

Others: means individuals other than Research Participants (e.g., Investigators, research assistants, students, the public, etc.).

Related (or “Possibly Related”): means that there is a reasonable possibility that the event, incident, experience or outcome may have been caused by the procedures involved in the Research, underlying disease, disorder, or condition of the Subject, or other circumstances unrelated to either the Research or any underlying disease, disorder, or condition of the Subject. Note that this is modified from the definition of associated with use of the drug in FDA regulations at 21 CFR §312.32(a).

Unanticipated Problem Involving Risks to Participants or Others: means any incident, experience, outcome, or new information where all three elements exist:

1. Is Unexpected;

2. Is Related or Possibly Related to participation in the Research, and

3. Indicates that subjects or Others are at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Unexpected: means the incident, experience or outcome is not expected (in terms of nature, severity, or frequency) given the Research procedures that are described in the Protocol-
related documents, such as the IRB-approved research Protocol and informed consent documents; and the characteristics of the subject population being studied;

### 8.3 Procedures

#### 8.3.1 Reporting

Investigators must promptly report the following problems to the IRB:

1. **Adverse Events** which in the opinion of the PI meet the criteria for an Unanticipated Problem involving risk to subjects or Others.

2. **An unanticipated event related to the Research** that exposes Participants to potential risk

3. **An unanticipated event related to the Research** that exposes individuals other than the research Participants (e.g., Investigators, research assistants, students, the public, etc.) to potential risk.

4. **Information that indicates a change to the risks or potential benefits of the Research.** For example:

   An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than initially presented to the IRB.

   A paper is published from another study that shows that the risks or potential benefits of your Research may be different than initially presented to the IRB.

5. **A breach of confidentiality**

6. **Incarceration of a Participant in a Protocol not approved to enroll Prisoners.**

7. **Change to the Protocol** taken without prior IRB review to eliminate an apparent immediate hazard to a research Participant.

8. **Complaint of a Participant** when the complaint indicates unexpected risks or cannot be resolved by the research team

9. **Protocol violation** (meaning an accidental or unintentional change to the IRB approved Protocol) that harmed Participants or Others or that indicates Participants or Others may be at increased risk of harm.

10. **Sponsor imposed suspension for risk**
11. Any other event that indicates Participant or Others might be at risk of serious, unanticipated harms that are reasonably related to the Research.

8.3.2 Submission of Reports
For Unanticipated Problems at a Tulane site (or at a Non-Tulane Site where Tulane is IRB-of-Record), 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.

For Unanticipated Problems *not* at a Tulane Site (i.e., external), Tulane’s IRB will accept event reports from a non-Tulane site (e.g., not University or TUHC premises) submitted by Investigators, study sponsors or the FDA on behalf of Investigators, provided the following conditions are met [FDA 21 CFR 312.32]:

- Tulane IRB recognizes that for multi-center studies, the Sponsor is in a better position to process and analyze unanticipated event information for the entire study, and to assess whether an occurrence is an Unanticipated Problem for the Study. Accordingly, Investigators may rely on the Sponsor’s assessment and provide the Sponsor’s assessment to the IRB using Tulane’s Unanticipated Problem Report Form (together with sponsor-provided reports).

The IRB will not accept non-Tulane site reports that do not meet Tulane’s reporting requirements.
Section 9 of the Tulane University HRPO SOPs:

Protocol Violations, Deviations, and Exceptions

9.1 Definitions

Protocol Deviation(s): means a minor or administrative departure from the IRB-approved Protocol procedures (e.g., the Protocol, informed consent document, recruitment process or study materials) that was made without prior sponsor and IRB approval. It is an accidental or unintentional change to, or non-compliance with the Research Protocol that neither (a) increases the risk or decreases the benefit; and (b) significantly affects the subject’s rights, safety or welfare and/or the integrity of the Research data. [Not defined by Common Rule or FDA regulations].

Protocol Exception (or “Exception”): means an impermanent (temporary) Protocol deviation that is pre-approved by the sponsor or funding agency, (and the FDA, if applicable, for investigational device studies) and the IRB prior to its implementation. Protocol Exceptions are generally for a single subject (e.g., the patient/subject is allergic to one of the medications provided as supportive care) or, occasionally, a small group of subjects. The Protocol Exception is usually evaluated by both the sponsor or funding agency (and FDA, if applicable) and the IRB in order to determine that it does not increase the risk to the subject (s), or jeopardize the integrity of the research data. Documentation of sponsor (or FDA) pre-approval and IRB approval of the exception should be maintained in the investigator’s research study file.

Protocol Violation(s): means an accidental or unintentional change to, or non-compliance with the IRB-approved procedures (e.g., the Protocol, informed consent document, recruitment process or study materials) without prior sponsor and IRB approval. Protocol Violations generally increases risk and/or decrease the benefit; affect the subject’s rights, safety or welfare and/or the integrity of the Research data. This term is not defined by the Common Rule or FDA regulations.

9.2 Planned Changes to Research Protocol

With regard to planned changes to a Research Protocol, the most common occurs through the submission of an amendment. Examples include an increase in subject number, changes in Investigators or key personnel, a change to the funding source, changes in procedures, revised consent documents and revised HIPAA Authorization. These all involve planned changes through an amended Protocol and are not Protocol Deviations themselves (although they may result from a Protocol Deviation).

Another type of planned change to the Research is called a Protocol Exception, which is made for a single subject or a small group of subjects, but is not a permanent revision to the research Protocol. Protocol Exceptions are a subset of Protocol Deviations. Similar to an amendment, a Protocol Exception must be IRB approved prior to its implementation. If the Research involves
an investigational Agent (e.g., Drug, Device, or Biologic), except in an emergency situation to eliminate immediate harm, prior approval by the sponsor also is required. Additionally, when Research involves an Investigational Device and the changes or deviations may affect the scientific soundness of the Research plan or rights, safety, or welfare of subjects, FDA and IRB pre-approval is required [21 CFR §812.150(4)]. Although a Protocol Exception must be prospectively approved by IRB, because the change does not involve a permanent change to the research Protocol, the FDA considers it to represent a Protocol Deviation.

Another type of planned change to a Protocol is a change made to eliminate apparent immediate harm to a subject. This type of change can be initiated without prior IRB approval, provided that subsequent IRB approval is obtained. These planned changes are a subset of Protocol Deviations.

9.3 Unplanned Changes to Research Protocol

The next category involves unplanned changes to a Research Protocol not otherwise approved by the IRB. Such unplanned changes are either Protocol Deviations or Protocol Violations. These unplanned changes may include changes of the IRB-approved Research Protocol, Good Clinical Practice (GCP) guidelines, regulatory standards, or Tulane’s HRPP.

9.4 Protocol Deviations:

A Protocol Deviation is any change or alteration from the procedures stated in the study Protocol, consent document, recruitment process, or study materials (e.g. questionnaires) originally approved by the IRB (but the change or alteration itself is not IRB-approved). Protocol Deviation is a general term and includes, Protocol Exceptions, changes made to avoid immediate harm to subjects, and Protocol Violations. [45 CFR §46.103 (b) (4) (iii), 21 CFR §56.108 (a) (4)]. Protocol Deviations can be either major or minor. Protocol Deviations can be examples of non-compliance, either non-serious or serious.

Repeated failure by a PI to not report Protocol Deviations may be viewed as non-compliance with the Federal regulations, the guidelines that govern ethical conduct of Research, and Tulane’s HRPP.

9.5 Protocol Violation:

A Protocol Violation is a subset of Protocol Deviation. It is any planned or unintended change or deviation from the IRB approved study Protocol, consent document, recruitment process, or study materials that were not approved by the IRB prior to implementation. Generally, Protocol Violations occur after the subject is enrolled in the Research. However, some Protocol Violations, such as deviations from the approved consent process, can occur before the subject is enrolled in the Research. Protocol Violations may be either Major Protocol Violations or Minor Protocol Violations, based on their relative severity.

9.6 Major Protocol Violation:

A Major Protocol Violation is a deviation that has an impact on subject safety, may substantially alter risks to subjects, may have an effect on the integrity of the study data, or may affect the
subject’s willingness to participate in the study. Major Protocol Violations can vary in the degree of seriousness according to how the changes impact subject safety, the degree of non-compliance with Federal regulations, State laws, the HRPP, Tulane policies or procedures, and the degree of foreknowledge of the event.

All Major Protocol Violations must be reported by the PI to the IRB within five (5) working days of learning of the violation. Use the Protocol Deviation/Violation/Exception Form to report Major Protocol Violations. If it is necessary to make a permanent change to the study procedures in order to avoid harm to other subjects, then a Protocol amendment should be submitted as soon as possible by the PI, using an Application for Amendment. If appropriate to maintain safety of the subjects, new subject enrollment should be temporarily stopped by the PI until the amendment is approved. No matter who discovers a Major Protocol Violation (e.g., sponsor or their agent during a monitoring visit), the PI is responsible for reporting it to the IRB.

9.7 Minor Protocol Violation:
A Minor Protocol Violation is one that does not impact subject safety, compromise the integrity of the study data, or affect the subject’s willingness to participate in the study.

No matter who discovers a Minor Protocol Violation (e.g., sponsor or their agent during a monitoring visit), the PI is responsible for reporting it to the IRB.

All Minor Protocol Violations do not require prompt reporting and should be reported by the PI to the IRB within ten (10) working days (or no later than at the time of continuing review) of learning of the violation. Use the Protocol Deviation/Violation/Exception Form to report Minor Protocol Violations.

9.8 Protocol Exception:
A Protocol Exception is an impermanent (temporary) Protocol Deviation that is reapproved by the sponsor or funding agency, (and, if applicable, the FDA for Investigational Device studies) and the IRB, prior to its implementation. Protocol Exceptions are generally for a single subject or, occasionally, a small group of subjects.

Protocol Exceptions must be submitted to IRB and granted approval prior to subject enrollment and implementation, except where necessary to eliminate apparent immediate hazards to the Human Subjects. [DHHS 45 CFR §46.103(b)(4); FDA 21 CFR §56.108(a)(4); ICH 3.3.7].

The Protocol Exception is usually evaluated by both the sponsor or funding agency (and the FDA, if applicable) and the IRB in order to determine that it does not increase the risk to the subject(s), or jeopardize the integrity of the research data. Documentation of sponsor (or FDA) pre-approval and IRB approval of the exception should be maintained in the PI’s Research Records. If the Research involves an Investigational Device, and the changes or deviations may 146
affect the scientific soundness of the plan or the rights, safety, or welfare of the Human Subjects, FDA pre-approval is also required [21 CFR §812.150 (4)].

The PI has ultimate responsibility for obtaining prior IRB approval for Protocol Exceptions. Repeated failure to obtain prospective IRB approval for Protocol Exceptions may be viewed as non-compliance with the Federal regulations, the guidelines that govern ethical conduct of Research, and Tulane’s HRPP.
Guidance for Clinical Investigators, Sponsors, and IRBs
Adverse Event Reporting to IRBs — Improving Human Subject Protection

Additional copies are available from:

Office of Training and Communication
Division of Drug Information, HFD-240
Center for Drug Evaluation and Research
Food and Drug Administration
(Tel) 301-827-4573
http://www.fda.gov/cder/guidance/index.htm
and/or
Office of Communication, Training and Manufacturers Assistance, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
(Tel) 800-835-4709 or 301-827-1800
and/or
Office of Communication, Education, and Radiation Programs
Division of Small Manufacturers, International, and Consumer Assistance (HFZ-220)
Center for Devices and Radiological Health
Food and Drug Administration
http://www.fda.gov/cdrh/ggpmain.html
Email: dcmica@cdrh.fda.gov; Fax: 301.443.8818
(Tel) Manufacturers Assistance: 800.638.2041 or 301.443.6597
(Tel) International Staff Phone: 301.827.3993

U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner (OC)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Good Clinical Practice Program (GCPP)
January 2009
Procedural
TABLE OF CONTENTS

I. INTRODUCTION .................................................................................................................. 1

II. BACKGROUND .................................................................................................................. 2

III. REPORTING AEs TO IRBs IN CLINICAL TRIALS OF DRUG AND BIOLOGICAL PRODUCTS CONDUCTED UNDER IND REGULATIONS .......... 3
    A. How to Determine If an AE is an Unanticipated Problem that Needs to Be Reported .... 3
    B. How to Report Unanticipated Problems to IRBs ............................................................ 5

IV. REPORTING AEs TO IRBs IN CLINICAL TRIALS OF DEVICES UNDER THE IDE REGULATIONS ................................................................. 6

V. CONCLUSION .................................................................................................................... 6
Guidance for Clinical Investigators, Sponsors, and IRBs
Adverse Event Reporting to IRBs — Improving Human Subject Protection

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This guidance is intended to assist the research community in interpreting requirements for submitting reports of unanticipated problems, including certain adverse events reports, to the institutional review board (IRB) under Title 21 of the Code of Federal Regulations (21 CFR) part 56 (Institutional Review Boards), part 312 (Investigational New Drug Application), and part 812 (Investigational Device Exemptions). Specifically, the guidance provides recommendations for sponsors and investigators conducting investigational new drug (IND) trials to help them differentiate between those adverse events that are unanticipated problems that must be reported to an IRB and those that are not. The guidance also makes suggestions about how to make communicating adverse events information to IRBs more efficient.

FDA developed this guidance in response to concerns raised by the IRB community, including concerns raised at a March 2005 public hearing, that increasingly large volumes of individual adverse event reports submitted to IRBs—often lacking in context and detail—are inhibiting, rather than enhancing, the ability of IRBs to protect human subjects.

FDA regulations use different terms when referring to an adverse event. For example, adverse effect is used in 21 CFR 312.64; adverse experience is used in § 312.32; and unanticipated problems is used in § 312.66. For the purposes of this guidance, the term adverse event is used, except when quoting specific regulations. For device studies, part 812 uses the term unanticipated adverse device effect, which is defined in 21 CFR 812.3(s).

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should

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1 This guidance has been prepared by the Office of the Commissioner, the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), the Center for Devices and Radiological Health (CDRH), and the Good Clinical Practice Program (GCPP) at the Food and Drug Administration.

be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

FDA regulates clinical studies authorized under sections 505(i) (drugs and biologics) and 520(g) (devices) of the Federal Food, Drug, and Cosmetic Act. All such clinical studies must be reviewed and approved by an IRB before the study is initiated, in accordance with the requirements of 21 CFR part 50 (Protection of Human Subjects), part 56 (Institutional Review Boards), and either part 312 (Investigational New Drug Application) or part 812 (Investigational Device Exemptions) (see §§ 50.1, 56.101, 312.23(a)(1)(iv), 312.40(a), 812.2(b)(1)(ii), 812.2(c) and 812.62(a)).3 After the initial review and approval of a clinical study, an IRB must conduct continuing review of the study at intervals appropriate to the degree of risk presented by the study, but at least annually (§ 56.109(b)). The primary purpose of both initial and continuing review of the study is “to assure the protection of the rights and welfare of the human subjects” (§ 56.102(g)). To fulfill its obligations during the conduct of a clinical study, an IRB must have, among other things, information concerning unanticipated problems involving risk to human subjects in the study, including adverse events (AEs) that are considered unanticipated problems (§§ 56.108(a)(3), (4), (b)).4

For clinical investigations of drug and biological products conducted under an investigational new drug (IND) application, information about adverse events5 must be communicated among investigators, sponsors, and IRBs as follows:

• Investigators are required to report promptly “to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. If the adverse effect is alarming, the investigator shall report the adverse effect immediately” (§ 312.64(b)).

• Sponsors are specifically required to notify all participating investigators (and FDA) in a written IND safety report of “any adverse experience associated with the use of the drug that is both serious and unexpected” and “any finding from tests in laboratory animals that suggests a significant risk for human subjects” (§ 312.32(c)(1)(i)(A),(B)). And, more generally, sponsors are required to “keep each participating investigator informed of new observations discovered by or reported to the sponsor on the drug, particularly with respect to adverse effects and safe use” (§ 312.55(b)).

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3 As described below, there are some differences between the requirements for investigational new drug and investigational device exemption studies, as they concern obligations to report to a reviewing IRB.
4 Unanticipated problems may be adverse events or other types of problems, i.e., adverse events are a subset of unanticipated problems.
5 The IND regulations use the term adverse effect (§ 312.64) and adverse experience (§ 312.32). These terms are interchangeable with adverse event.
contains nonbinding recommendations

- Investigators are required to report promptly “to the IRB... all unanticipated problems involving risks to human subjects or others,” including adverse events that should be considered unanticipated problems (§§ 56.108(b)(1), 312.53(c)(1)(vii), and 312.66).

A critical question for studies conducted under part 312 is what adverse events should be considered unanticipated problems that merit reporting to an IRB. In the years since the IRB and IND regulations issued, changes in the conduct of clinical trials (e.g., increased use of multi-center studies, international trials) have complicated the reporting pathways for adverse event information described in the regulations. In particular, the practice of local investigators reporting individual, unanalyzed events to IRBs, including reports of events from other study sites that the investigator receives from the sponsor of a multi-center study—often with limited information and no explanation of how the event represents an unanticipated problem—has led to the submission of large numbers of reports to IRBs that are uninformative. IRBs have expressed concern that the way in which investigators and sponsors of IND studies typically interpret the regulatory requirement to inform IRBs of all "unanticipated problems" does not yield information about adverse events that is useful to IRBs and thus hinders their ability to ensure the protection of human subjects. This guidance is intended to help differentiate those adverse events that should be considered unanticipated problems (and thus reported to the IRB) from those that should not, thereby helping to ease the burden on IRBs and make the adverse events information they receive more informative and useful.

III. REPORTING AEs TO IRBs IN CLINICAL TRIALS OF DRUG AND BIOLOGICAL PRODUCTS CONDUCTED UNDER IND REGULATIONS

A. How to Determine If an AE is an Unanticipated Problem that Needs to Be Reported

In general, an AE observed during the conduct of a study should be considered an unanticipated problem involving risk to human subjects, and reported to the IRB, only if it were unexpected, serious, and would have implications for the conduct of the study (e.g., requiring a significant, and usually safety-related, change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, informed consent, or investigator’s brochure). An individual AE occurrence ordinarily does not meet these criteria because, as an isolated event, its implications for the study cannot be understood.

Many types of AEs generally require an evaluation of their relevance and significance to the study, including an aggregate analysis of other occurrences of the same (or similar) event, before they can be determined to be an unanticipated problem involving risk to human subjects. For example, an aggregate analysis of a series of AEs that are commonly associated with the underlying disease process that the study intervention is intended to treat (e.g., deaths in a cancer trial), or that are otherwise common in the study population independent of drug exposure (e.g., cardiovascular events in an elderly population) may reveal that the event rate is higher in the drug treatment group compared to the control arm. In this case, the AE would be considered an unanticipated problem. In the absence of such a finding, the event is uninterpretable.
The major exceptions to the general rule that an isolated event is not informative are serious AEs that are uncommon and strongly associated with drug exposure, such as angioedema, agranulocytosis, anaphylaxis, hepatic injury, or Stevens Johnson syndrome. In most cases, a single, unexpected occurrence of this type of event would be considered an unanticipated problem involving risk to human subjects and, thus, must be reported to the IRB. Similarly, one or a small number of serious events that are not commonly associated with drug exposure, but are otherwise uncommon in the study population (e.g., tendon rupture, progressive multifocal leukoencephalopathy) should be considered an unanticipated problem involving risk to human subjects.

Because they have been previously observed with a drug, the AEs listed in the investigator’s brochure would, by definition, not be considered unexpected and thus would not be unanticipated problems. Possible exceptions would include situations in which the specificity or severity of the event is not consistent with the description in the investigator’s brochure, or it can be determined that the observed rate of occurrence for a serious, expected AE in the clinical trial represents a clinically important increase in the expected rate of occurrence.

Therefore, FDA recommends that there be careful consideration of whether an AE is an unanticipated problem that must be reported to IRBs. In summary, FDA believes that only the following AEs should be considered as unanticipated problems that must be reported to the IRB.

- A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure (such as angioedema, agranulocytosis, hepatic injury, or Stevens-Johnson syndrome).
- A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with drug exposure, but uncommon in the study population (e.g., tendon rupture, progressive multifocal leukoencephalopathy).
- Multiple occurrences of an AE that, based on an aggregate analysis, is determined to be an unanticipated problem. There should be a determination that the series of AEs represents a signal that the AEs were not just isolated occurrences and involve risk to human subjects (e.g., a comparison of rates across treatment groups reveals higher rate in the drug treatment arm versus a control). We recommend that a summary and analyses supporting the determination accompany the report.
- An AE that is described or addressed in the investigator’s brochure, protocol, or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations. For example, if transaminase elevation is listed in the investigator’s brochure and hepatic necrosis is observed in study subjects, hepatic necrosis would be considered an

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6 An unexpected adverse drug experience is defined as "[a]ny adverse drug experience, the specificity or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the investigator brochure only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the investigator brochure only listed cerebral vascular accidents. Unexpected, as used in this definition, refers to an adverse drug experience that has not been previously observed (e.g., included in the investigator brochure), rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product." (21 CFR 312.32(a))
Contains Nonbinding Recommendations

unanticipated problem involving risk to human subjects. We recommend that a discussion of the divergence from the expected specificity or severity accompany the report.

- A serious AE that is described or addressed in the investigator’s brochure, protocol, or informed consent documents, but for which the rate of occurrence in the study represents a clinically significant increase in the expected rate of occurrence (ordinarily, reporting would only be triggered if there were a credible baseline rate for comparison). We recommend that a discussion of the divergence from the expected rate accompany the report.

- Any other AE or safety finding (e.g., based on animal or epidemiologic data) that would cause the sponsor to modify the investigator’s brochure, study protocol, or informed consent documents, or would prompt other action by the IRB to ensure the protection of human subjects. We recommend that an explanation of the conclusion accompany the report.

B. How to Report Unanticipated Problems to IRBs

In a multicenter study, it is clear that individual investigators must rely on the sponsor to provide them information about AEs occurring at other study sites. It is also clear that the sponsor receives AE information from all study sites and typically has more experience and expertise with the study drug than an investigator. Accordingly, the sponsor is in a better position to process and analyze the significance of AE information from multiple sites and—when the determination relies on information from multiple study sites or other information not readily accessible to the individual investigators (e.g., a sponsor’s preclinical data that supports the determination)—to make a determination about whether an AE is an unanticipated problem. Furthermore, the regulations require the sponsor of an IND to promptly review all information relevant to the safety of the drug and to consider the significance of the report within the context of other reports (§ 312.32).

The regulations state that for studies conducted under 21 CFR part 312, investigators must report all "unanticipated problems" to the IRB (§§ 312.66, 312.53(c)(1)(vii), and 56.108(b)(1)). However, as discussed above, we recognize that for multicenter studies, the sponsor is in a better position to process and analyze adverse event information for the entire study and to assess whether an adverse event occurrence is both unanticipated and a problem for the study.

Accordingly, to satisfy the investigator’s obligation to notify the IRB of unanticipated problems, an investigator participating in a multicenter study may rely on the sponsor's assessment and provide to the IRB a report of the unanticipated problem prepared by the sponsor. In addition, if the investigator knows that the sponsor has reported the unanticipated problem directly to the IRB, because the investigator, sponsor, and IRB made an explicit agreement for the sponsor to report directly to the IRB, and because the investigator was copied on the report from the

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7 Section 312.32(c)(1)(ii) requires a sponsor preparing an IND safety report to, among other things, “analyze the significance of the adverse experience in light of previous, similar reports.” Section 312.32(b) requires the sponsor to “promptly review all information relevant to the safety of the drug obtained or otherwise received by the sponsor from any source . . . .”

8 Note that such an agreement would be required to be incorporated into the IRB’s written procedures (21 CFR 56.108(b)(1), 56.115(a)(6)).
IV. REPORTING AEs TO IRBs IN CLINICAL TRIALS OF DEVICES UNDER THE IDE REGULATIONS

The investigational device exemption (IDE) regulations define an unanticipated adverse device effect (UADE) as “any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects” (21 CFR 812.3(s)). UADEs must be reported by the clinical investigator to the sponsor and the reviewing IRB, as described below:

- For device studies, investigators are required to submit a report of a UADE to the sponsor and the reviewing IRB as soon as possible, but in no event later than 10 working days after the investigator first learns of the event (§ 812.150(a)(1)).

- Sponsors must immediately conduct an evaluation of a UADE and must report the results of the evaluation to FDA, all reviewing IRBs, and participating investigators within 10 working days after the sponsor first receives notice of the effect (§§ 812.46(b), 812.150(b)(1)).

The IDE regulations, therefore, require sponsors to submit reports to IRBs in a manner consistent with the recommendations made above for the reporting of unanticipated problems under the IND regulations.

V. CONCLUSION

The receipt of a large volume of individual AE reports without analysis of their significance to a clinical trial rarely supports an IRB’s efforts to ensure human subject protection. Sponsors can assess the implications and significance of AE reports promptly and are required to report serious, unexpected events associated with the use of a drug or device, including analyses of such events, to investigators and to FDA. In addition, sponsors are required to report analyses of unexpected adverse device experiences to IRBs. FDA encourages efforts by investigators and sponsors to ensure that IRBs receive meaningful AE information. The ultimate goal is to provide more meaningful information to IRBs, particularly when sponsor analysis (including an analysis of the significance of the adverse event, with a discussion of previous similar events where appropriate) is made available to IRBs.