# Office of Human Research Ethics Training Tips: Deferral of Studies

***"OPRR recommends the following guidelines in such cases:***

***(i) When the convened IRB requests substantive clarifications, protocol modifications, or informed consent document revisions, IRB approval of the proposed research must be deferred, pending subsequent review of responsive materials by the convened IRB.***

***(ii) Only when the convened IRB stipulates specific revisions requiring simple concurrence by the investigator may the IRB chair or designated reviewer subsequently approve the research on behalf of the IRB."***

**THE *'-ATION''* LIST**

**A protocol may be deferred if any of the following are required during review by a convened IRB:**

**Elabor*ation***

**Clarific*ation***

**Document*ation***

**Explan*ation***

**Justific*ation***

**Modific*ation***

**Adapted from Joseph F. Farmer, MD**

- ***To clarify*** - (paragraph 2) - your hypothesis is that…… **[See 111 Criteria #1]**

- Is there any evidence currently that characterizes the relationship between……**See 111 Criteria #1]**

- What is the rationale for studying nine analytes? **[See 111 Criteria #1]**

- What is your hypothesis for the inflammatory profile? **[See 111 Criteria #1]**

- ***Clarification*** about the choice of study is necessary - why is this a cross-sectional study of 30 participants which is not going to provide ample information. Please list all the specific aims and match the analysis plans to them.

- The list of specific aims in this section is incomplete. Furthermore the stated specific aims are not closely matched with the statistical analysis plans.

- please ***clarify*** reduction in number of participants from 45 to 30 ***(are 30 subjects enough to answer the research question?)***

- Will it be fasting or non-fasting maternal blood?

- What is the interobserver variability in this measures?

- ....since they are not expected to be normally distributed - please revise this sentence. **[MUST provide the exact sentence for the PI to use.]**

- As this study entails x-rays for research purposes only, and the consent form indicates that pregnant women may be "precluded", it is assumed that this means excluded from the study. Assuming this to be true, please revise this answer and the exclusion criteria in A.3.1 to reconcile the responses, and clarify consent language regarding pregnancy, and indicate how you will test for pregnancy in females (urine test, for example).

- No one from Sport and Exercise Science is listed among the project personnel. As several of your outcome measures will be obtained by graduate students in Sport and Exercise Science, please include a faculty member from that department who will supervise the students***. [This is fine, they are asked to add the name of faculty from Sport & Exercise Science; so the staff & chairs can easily see if that is done. Once faculty name added to the study, then it can be approved. UNLESS there are other changes required by the IRB.]***

- You indicate that subjects will only participate in one session. But here you say you will mail results to subjects (which obviously must be some time after the subjects' single session), and that they will have an "opportunity to discuss results."

    - How and when can they discuss these results with the resident physician?
    - Will they have to come in for a second session?
    - Will there be a follow-up session by phone?" **Please clarify.**

- Please address the process for identifying incidental findings on the radiographic exam. If a new fracture or other issue is identified, explain how (and how soon) the participant will be notified.

- Please provide a plan for ensuring data quality. **[** ***See 111 Criteria #6*** *]*

## Criteria for IRB Approval of Research
## §46.111 & §56.111

(a) In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:

(1) Risks to subjects are minimized:

(i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, **and**

(ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

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

In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research).

The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment the IRB should take research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disable persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §46.116.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117.

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(b) When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

# Human Research Ethics Training Tips

## Guide for Writing Clear, Concise Stipulations for Investigators

### Guide for Writing Clear, Concise Stipulations Sent to Investigators

### #1. Write stipulations in a professional, respectful manner.

- ***Original stip:*** The details and discussion of *X* were poorly written and ambiguous.
- **Guidance:** Remember, the IRB correspondence is directed to the study PI. Write, "Please revise…" instead of, "The researcher should revise…"
- ***Revised stip:*** Please provide a more robust discussion of *X* with particular attention to the details and of *Y*.

### #2. Write stipulations as complete sentences, using proper grammar and correct spelling. Do not use abbreviations that may be unclear to the researcher.

- **Original stip:** Will need non-English consents, if applicable.
- **Revised stip**: Because you plan to enroll non-English speaking subjects, please submit non-English consent forms.
    - If the researcher used the abbreviations in the application, you may use those in your stipulations; do not use abbreviations that may be unfamiliar to the researcher.

### #3. Write stipulations as clear, *directive* sentences. If a stipulation is a *recommendation*, clearly state that.

- ***Original stip***: Because of the renal toxicity associated with Cisplatin, a GFR measurement rather than 1.5X ULN creatinine would be more realistic as a measure of renal function.
- ***Revised stip:*** Because of renal toxicity associated with Cisplatin, the IRB recommends using a GFR measurement rather than creatinine. Please either revise or provide a strong rationale for retaining urine creatinine as a measure of renal function.

### #4. Pair each stipulation with the appropriate IRBIS question.

- ***Original stip:*** A.4.2 (Study design): Please describe who will read the ultrasound and their qualifications for using and evaluating an ultrasound.
- ***Recommendation:*** Move stip to A.4.7 (Specialized training) Refrain from entering stipulations as *global stipulations* if the stipulation is in reference to a specific IRBIS question.
- ***Acceptable global stipulation***: *Please spell out all acronyms the first time they are used.*

*This is very important.* *It takes a lot of extra time on the part of the IRB Analyst to move stipulations to the proper sections of the application. Remember, that in most cases, the researcher not only responds to the stipulation but is also required to revise that section of the application. If you stip in the wrong section, their revisions will also be in the wrong section.*

## #5. Combine similar or duplicate stipulations.

- ***Original stips:***
  Please provide additional comment on minimizing potential risks regarding disclosure of illegal activity.

- Please mark "disclosure of illegal activity" as drug testing may identify individuals using illegal drugs.

- ***Combined stip:***
  As drug testing may identify individuals who use illegal drugs, please mark "disclosure of illegal activity" and describe what will be done to minimize this risk.

- If someone else has already entered a similar stipulation, either do not add a second stip be clear that your stipulation is meant to add the first stip.

## #6. Provide context to support stipulations.

- ***Original stip:*** Please respond "yes" to this question.

- **Revised stip**: The master protocol states that you will be collecting HIV status at baseline therefore you should change your response here to "yes".

- ***Very important!*** Without context, the research may not understand why you are asking for a change. Whenever possible, provide context or reference to protocol or application. (e.g., Disaster protocol, page 27, states, "abc..." but here you state "def...", please revise for concordance.)

## #7. If the information is complete and accurate, refrain from *stipping* about *how* the information is presented. *No wordsmithing!*

- ***Original stip:*** The response is written in second person (as if consenting a participant). Please revise the response to 3rd person. Although this information appears to be copied from the consent form, if accurate and complete, do not stip.

- **WHAT** information is provided is much more important that **HOW** the information is provided.

## #8. Do not offer options that cannot be approved.

- ***Original stip:*** On page 10 of the ICF, subjects are told they can decline the pharmacogenetic blood draw at Visit 1 and still be in the study. The ICF for stored samples does not list a "no blood draw" option. Will the pharmacogenetic blood draw opt-out be a verbal decline? Please clarify/reconcile.

- ***Guidance:*** Delete underlined sentence as this is not a viable option (i.e., not approvable). Instead, if optional, instruct PI to add "yes/no" option for pharmacogenetic blood draw on the signature page.

- ***Revised stip:*** If the pharmacogenetic blood draw is optional, please add a "yes/no" option on the signature page of the main consent form.

## #9 Anticipate more than one response and write stipulation to cover all possibilities.

- ***Original stip:*** Will parents be notified of positive pregnancy tests of those <18 years old? If so, this should be specifically stated in the Assent forms and Parental consent forms.

- ***Guidance:*** NC law does not require that parents be informed of the results of pregnancy testing of minors. However, if pregnancy testing is conducted as part of a research study, we require both parents/guardians and minor subjects be informed about whether or not the results will be shared.

- ***Revised stip:*** Will parents be notified of positive pregnancy tests of those <18 years old? Please include a statement in both the parental permission and minor assent forms *whether or not* pregnancy test results will be shared with parents.

## Final Notes:

- **Write the stip you would want to receive it—be clear what the question is and what the IRB is asking to be changed.**

- **If you do #1, then there is no misunderstanding by the investigator nor misunderstanding when revision is reviewed by staff & chair.**

- **And no misunderstanding that the stip revision can be expedited and instead is a deferral that must be returned to the IRB for review, discussion and vote.**