PROTOCOL REVIEWS

HOW TO CONDUCT SYSTEMATIC, COMPREHENSIVE & EFFICIENT REVIEWS
THE WORK **BEFORE** THE MEETING

- Review your assigned protocols well before the meeting and provide written comments in RAMS-IRB.

- Consider the IRB meeting to be primarily a place to **make decisions**, not gather information.

- Get your questions answered **before** the meeting from IRB staff and the PI and study team. Questions to the study team can be coordinated with the IRB Administrator.
THE WORK BEFORE THE MEETING

- If you want the investigator to make specific changes in language to a particular document (i.e. Informed consent, protocol, etc.), come to the meeting with the changes marked on the current document so that the document reads as you would like it to read after the changes.

- Do not ask the study team to make these changes prior to the meeting as all changes must be voted on by the full IRB.
REVIEWING NEW SUBMISSIONS (PRIMARY REVIEWER ROLE)

- Use a systematic approach to review the submission materials
- The following approach is outlined in your Member Handbook
REVIEWING NEW SUBMISSIONS
(PRIMARY REVIEWER ROLE)

- Read the informed consent document, without taking notes, to get a general feel for the study
REVIEWING NEW SUBMISSIONS (PRIMARY REVIEWER ROLE)

- Read the full protocol and any applicable supporting materials including the RAMS-IRB SmartForm
  - This will provide you with the total picture and may also indicate any discrepancies between the summary and the full protocol, or the summary, ICF and the full protocol
  - This will also provide increased detail as related to study procedures, design, etc.
REVIEWING NEW SUBMISSIONS (PRIMARY REVIEWER ROLE)

- Read the informed consent document again
  - Now that you are aware of the contents of the protocol, RAMS-IRB SmartForm and any additional materials, consider the following:
    - Does the ICF provide a fair and informative presentation of the study’s objectives, purpose, procedures, risks, benefits and any other necessary information?
    - Are all required elements of consent covered?
REVIEWING NEW SUBMISSIONS (PRIMARY REVIEWER ROLE)

- The IRB has reviewer guidance documents available on the IRB website
- Please use these documents to guide your review and remind you of what specific items you should be considering while reviewing
- Consult the Completeness Checklist and IRB Staff Comments for additional items to consider.
ITEMS FOR CONSIDERATION DURING PRIMARY REVIEWER INITIAL REVIEW

INTRODUCTION, SPECIFIC AIMS, AND BACKGROUND

■ Are the specific aims clearly specified?
■ Are there adequate preliminary data to justify the research?
■ Is there appropriate justification for this research protocol?
SCIENTIFIC DESIGN

- Is the scientific design adequate to answer the question?
- Are the objectives likely to be achievable within a given time period?
- Is the scientific design (i.e. Randomization, placebo controls, Phase I, II or III) described and adequately justified?
  - NOTE: The IRB is not a scientific review board, so in general if design is appropriate and safe for human subjects, it likely meets the criteria for IRB approval. However, closer attention should be paid to studies that have not already been reviewed by an outside scientific review board (i.e. unfunded research)
ITEMS FOR CONSIDERATION DURING PRIMARY REVIEWER INITIAL REVIEW

INCLUSION/EXCLUSION CRITERIA FOR SUBJECTS

- Are inc/exc. criteria clearly specified and appropriate?
- If women, minorities, or children are included or excluded, is this justified?
- Is the choice of subjects appropriate for the question being asked?
- Is subject selection equitable?
ITEMS FOR CONSIDERATION DURING PRIMARY REVIEWER INITIAL REVIEW

RECRUITMENT OF SUBJECTS

- Are the methods for recruiting potential subjects well defined?
- Are the location and timing of the recruitment process acceptable?
- Is the individual performing the recruitment appropriate for the process?
- Are all recruitment materials submitted and appropriate?
- Are there acceptable methods for screening subjects before recruitment?
ITEMS FOR CONSIDERATION DURING PRIMARY REVIEWER INITIAL REVIEW

RESEARCH PROCEDURES

■ Are the rationale and details of the research procedures accurately described and acceptable?
■ Is there a clear differentiation between research procedures and standard of care?
■ Are the individuals performing the procedures appropriately trained and is the location for performance of procedures acceptable?
■ Are there adequate plans to inform subjects about specific research results if necessary?
ITEMS FOR CONSIDERATION DURING PRIMARY REVIEWER INITIAL REVIEW

DRUGS, BIOLOGICS, AND DEVICES

■ Is the status of the drug described and appropriate (i.e. use of investigational agent)?
■ Are the drug dosage and route of administration appropriate?
■ Are the drug and device safety and efficacy data sufficient to warrant the proposed phase of testing?
■ Is the significant risk or non-significant risk status of the device described and appropriate?

  – NOTE: Betsy Ripley is the Clinical Research Compliance Officer and IRB staff typically send PIs to her or consult her for information on whether a study requires an IND/IDE, it’s exempt, or a NSR determination is needed
ITEMS FOR CONSIDERATION DURING PRIMARY REVIEWER INITIAL REVIEW

DATA ANALYSIS AND STATISTICAL ANALYSIS

■ Is the rationale for the proposed number of subjects reasonable?
■ Are the plans for data and statistical analysis defined and justified, including the use of stopping rules and endpoints?
■ Are there adequate provisions for monitoring data (DSMB)?
ITEMS FOR CONSIDERATION DURING PRIMARY REVIEWER INITIAL REVIEW

POTENTIAL RISKS, DISCOMFORTS AND BENEFITS FOR SUBJECTS

- Are the risks and benefits adequately identified, evaluated and described?
- Are the potential risks minimized and likelihood of benefits maximized?
- Is the risk/benefit ratio acceptable for proceeding with the research?
- If children are involved, with regulatory category of risk/benefit does the protocol fall within and are all criteria within the category adequately addressed?
ITEMS FOR CONSIDERATION DURING PRIMARY REVIEWER INITIAL REVIEW

COMPENSATION AND COSTS FOR SUBJECTS

- Is the amount or type of compensation or reimbursement reasonable?
- Are there adequate provisions to avoid out-of-pocket expenses by the research subject, or is there sufficient justification to allow subjects to pay?
- If children or adolescents are involved, who receives the compensation and is this appropriate?
ITEMS FOR CONSIDERATION DURING PRIMARY REVIEWER INITIAL REVIEW

PRIVACY AND CONFIDENTIALITY

- Are there adequate provisions to protect privacy and ensure confidentiality of the research subject?
- Are there adequate plans to store and code the data?
- Is the use of identifiers or links to identifiers necessary, and how is this information protected?
OTHER ISSUES

■ Are adequate references provided?

■ When should the next review occur? If frequent reviews are necessary, how should the interval be determined?
REQUESTING CHANGES TO THE RESEARCH

- To help you focus your efforts when evaluating a research protocol and informed consent form, it may be useful to ask yourself this question:

  Is a change in the research protocol or consent form likely to improve the welfare of research subjects to a meaningful degree?

- If your answer to this question is "no," then you should approve the research proposal without changing it.

- If your answer to this question is "yes," then you should not approve the research plan as proposed.
REVIEWING NEW SUBMISSIONS
(SECONDARY REVIEWER ROLE)

Use a systematic approach to review the submission materials and focus on any materials the subjects will see or receive, such as the consent form, study instructions, recruitment materials, etc.

The following approach is outlined in your Member Handbook as well
REVIEW OF THE INFORMED CONSENT (SECONDARY REVIEWER)

THE FOLLOWING INFORMATION MUST BE INCLUDED PER FEDERAL REGS:

- Research purpose and procedures
- Risks and discomforts
- Potential benefits
- Alternative procedures or treatment
- Provisions for confidentiality
- Research-related injury
- Voluntary participation and the right to discontinue participation without penalty
- Contacts for additional information
REVIEW OF THE INFORMED CONSENT (SECONDARY REVIEWER)

WHEN APPROPRIATE, THE FOLLOWING ADDITIONAL INFORMATION SHOULD BE INCLUDED:

- Unforeseeable risks
- Termination of participation by the investigator
- Additional costs
- Consequences of discontinuing research participation
- Notification of significant new findings
- Approximate number of subjects to be enrolled
TIPS FOR REVIEWING CONSENTS:

Informed Consent

- Use the informed consent worksheet to guide your review.
- **Resist the urge to make unimportant changes to the ICF.**
- Any substantive changes/issues must be discussed at the meeting.
- Make the distinction between required and recommended changes to the consent form.
- Waivers or alteration of the consent form require discussion and documentation.
- Waivers of documentation of consent require discussion and documentation (e.g. the IRB must make a formal determination to waive documentation of consent for telephone screening)

HIPAA Authorization

- Verify that all required elements are presented in either the stand-alone or combined form.
  - **Note:** IRB staff will also check this during pre-screen
CONTINUING REVIEWS: TIPS

■ Determine if the study is progressing as planned
■ Determine if any unexpected events have occurred that may indicate a need for change to study documents
■ Consider any applicable documents to consider whether the study may continue as planned:
  - DSMB reports
  - Sponsor annual reports
  - AE/deviation logs
AMENDMENTS: TIPS

- Look for the summary of changes and consider whether appropriate rationale has been provided for the changes
- Determine whether the changes alter the risk/benefit profile for subjects
- Determine if the consent document has been appropriately revised (if applicable) and if the proposed plan for re-consent is appropriate
- Determine if the study continues to meet the criteria for approval with the changes that have been made
INITIAL REVIEW DECISIONS

- The Primary Reviewer is expected to make a recommendation to the committee for one of the following decisions:

  - **APPROVED** The criteria required for approval are deemed acceptable, protocol is approved as submitted.

  - **WITHHELD/CONDITIONAL APPROVAL** The IRB determines that the protocol will meet the regulatory criteria for approval provided the investigator agrees to make specific changes to the IRB application including the informed consent document.

  - **TABLED** The IRB requires substantive changes that are directly relevant to the determinations required by the IRB under federal regulations at §_.111, the IRB will table the approval of the protocol pending subsequent review by the convened IRB of the responsive material.

  - **DISAPPROVED** The IRB determines that the research does not meet the regulatory criteria for approval and cannot provide modifications that may allow the protocol to be approved.

  - **APPROVAL PERIOD** Continuing review at interval appropriate to degree of risk but not less than once per year. The IRB may also require observation of the consent process.
Limit the initial summary of your review to one to two minutes

Your presentation should consist of summarizing the study and your major concerns

Presentations by secondary reviewers should focus on the informed consent form and any disagreements with the primary review

End presentation with a vote recommendation
STIPULATIONS VS. RECOMMENDATIONS

- Stipulations require a response. The response must be very explicit regarding the required revisions.

- Recommendations do not require a response and/or revision. They are simply suggestions from the Board.