DF/HCC
DANA-FARBER / HARVARD CANCER CENTER

OHRS Office Hours

TOP 10 IRB CONDITIONS IN CONDITIONAL APPROVALS

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TOP TEN CONDITIONS FOR APPROVAL BY THE IRB: HOW TO SUBMIT NEW PROTOCOLS AND ICFs THAT MAKE IT THROUGH QUICKLY

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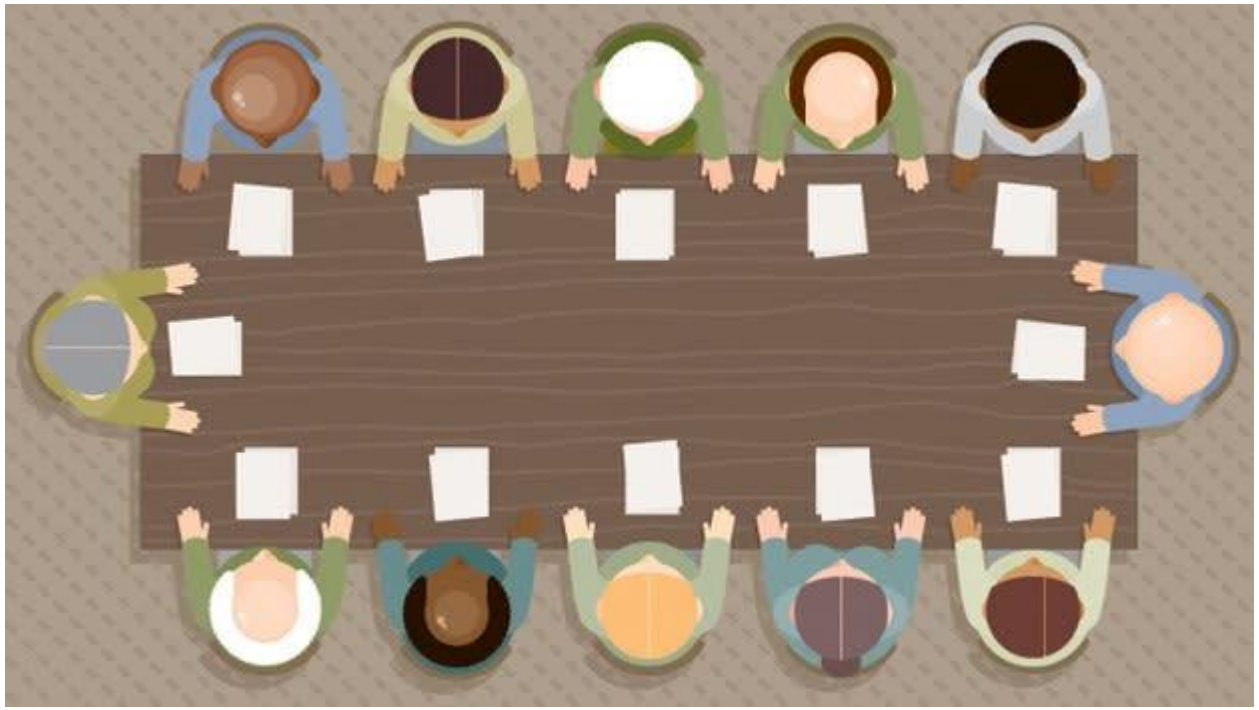

1. Use Lay Language for Risks and Side Effects

- Use language understandable to a lay reader
  - NCCN database provides definitions in lay terms for common side effects, lab tests, conditions
  - Include symptoms that may be experienced by the participant
  - All clinical research communications should be clear and easy to understand
- Use of animal data is difficult to interpret for a lay reader, avoid unless there is little or no human data; use “preclinical data” as preferred term

1. Use Lay Language for Risks and Side Effects

- Examples:

  Thrombocytopenia

- Recommendations:
  - Low number of platelets, which may cause bleeding and bruising. Bleeding may be serious or life threatening and may require a blood transfusion.

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- Sepsis, septic shock, peritonitis, lower respiratory tract infection, fungal infection, viral infection, bronchitis, abscess, cellulitis, influenza, gastrointestinal infection, sinusitis, tooth infection

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- Examples:

  "Depending on which arm of the study you are participating in, investigators will administer the chemotherapeutic agent to ascertain the number of difficulties you experience in reaction to the drug."

- Recommendations:
  - Simple Measure of Gobbledygook
  - Flesch-Kincaid
  - Plainlanguage.gov

2. Use “Participant” Instead of “Patient”

- To Avoid the “therapeutic misconception”
  - ‘Research participant’ or ‘research subject’ should be used when referring to the person from whom consent is being sought
  - Fosters the understanding of the distinction between clinical care and enrolling on a research protocol with often more limited options

3. Payment Plan is Not Clear

- Often the reimbursement plan has not been submitted
  - Include the basic plans for reimbursement and we can approve
- Important to distinguish between direct payment to participants or reimbursement for out-of-pocket costs to participants
- If it is not clear whether there will be a reimbursement plan or any specifics; consider waiting to add it by amendment if the specific plan is not known at the time of submission

3. Payment Plan is Not Clear

10.2 Participant Gifts/Payment

Please Note:

If providing compensation:

- The IRB will not approve a
  giving participants' gift ba
- Any amount over $600.00
- Please ensure the consent
  provided in totality at the

If providing reimbursement:

- Please outline exactly wha
  for subject remuneration,
- Reimbursement information must be in the consent form or additional patient facing information sheet.

Participants will be provided the following (check all that apply):

- ☐ Compensation – payment to participants for time, inconvenience, or incentive to participate. Compensation amounts should not be seen as unduly influencing the decision to participate.
- ☐ Reimbursement – paying back participants for travel expenses such as mileage, lodging, and food while traveling.
- ☑ No current plan to pay participants (e.g., payment is still being negotiated, or there is no plan to pay, payment details will be submitted upon future amendment)

F. WILL I BE PAID TO TAKE PART IN THIS RESEARCH STUDY?

You will not be paid for participating in this study.

The study sponsor may reimburse you for qualifying study-related travel costs and/or expenses. Study staff will review the reimbursement plan and any requirements for reimbursement with you.

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4. Remove or Replace Contractual Language

- "You must agree to …." or "You agree to…."
  - This should be replaced with "It is a protocol requirement…" (e.g., that you use an effective method of birth control such as …"
- Before the signature line the phrase "I agree…", "I understand…"

4. Remove or Replace Contractual Language

Examples:	Recommendations:
4. What does this research study involve and how long will it last? The name of the study drug involved in this study is: • ABC123 You must attend the following protocol visits: screening for eligibility and study treatment including evaluations and follow up visits.	**4. What does this research study involve and how long will it last?** The name of the study drug involved in this study is: • ABC123 The research protocol includes the following visits: screening for eligibility and study treatment including evaluations and follow up visits.

5. Risks Organized by Frequency

- Some exceptions (may not be enough data in early phase trials), but generally use a consistent frequency table
- Bullet formatting or other clear tables
- Explain or remove risks that appear in two frequencies
- Include risks of SOC arm or when SOC treatment is part of the protocol design (not treatment for side effects per clinical decision making)
- Decide what goes in the Key Information section

5. Risks Organized by Frequency

- Example:

<u>Risks Associated with ABC123:</u>

Likely (More than a 50% chance that this will happen)

Increased Infection Risk: Sepsis, septic shock, peritonitis, lower respiratory tract infection, fungal infection, viral infection, bronchitis, abscess, cellulitis, influenza, gastrointestinal infection, sinusitis, tooth infection, fungus infection, Bacterial arthritis, impetigo, gum disease

5. Risks Organized by Frequency

- Suggestion

Risks Associated with ABC123:

Likely (More than a 50% chance that this will happen)

- Sepsis, which is a serious condition that occurs in response to an infection that causes widespread inflammation, resulting in poor blood supply to vital organs. Symptoms may include a fast heart rate, fever, confusion and rapid breathing. Sepsis can rapidly lead to a life threatening clinical condition.
- Peritonitis, which causes abdominal wall inflammation.
- Lower respiratory tract infection, which may be fungal or viral and cause an increased risk of infection, such as pneumonia. This infection may occur anywhere. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and/or difficulty breathing.
- Bronchitis, which causes lung inflammation.
- Abscess, which is caused low blood cell counts (white blood cells). A low white blood cell count increases your risk of infection (such as pneumonia and/or severe blood infection). Infections may occur anywhere and become life-threatening. Symptoms of infection may include fever, pain, redness, and/or difficulty breathing.
- Cellulitis, is an infection of the skin. A low number of white blood cells may increase the risk of infection. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and/or difficulty breathing
- Influenza infection, which causes the “flu”.
- Gastrointestinal infection, which may cause digestive system problems.
- Sinusitis, is a sinus infection. Symptoms of infection may include fever, pain, redness, and/or difficulty breathing.
- Tooth Infection
- Bacterial arthritis, which may cause joint inflammation and swelling.
- Impetigo, which is a bacterial infection of the skin. This can cause a rash and sores on the skin.
- Gum disease, which can cause gum sores and gum bleeding.

6. Remove or Revise Exculpatory Language

- Frequently found in the In Case of Injury section
  - No waiving of their rights
  - Clearly state who will pay for treatment of injuries without extensive legal language around the conditions (can exclude underlying disease, and can say “directly” caused by the product or procedures in the protocol; or “properly followed protocol”
- Biospecimen “ownership”
  - No plans to pay you for commercial use, etc.
  - No waivers of rights

6. Remove or Revise Exculpatory Language

By agreeing to this use, you should understand that you will give up all claim to personal benefit from commercial or other use of these substances.

I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. Government and hereby relinquish all right, title, and interest to said items.

By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.

I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.

Samples may also be shared with outside non-profit academic investigators as well as with for-profit investigators or commercial entities, with whom we collaborate..

Your genetic data may also be placed into one or more publicly-accessible scientific databases. Researchers from around the world will have access to deidentified samples or data for future research.

Treatments may be billed to you or your insurance company. You will be responsible for deductibles, co-payments and co-insurance. There are no plans to pay you or give you other compensation for the injury.

7. Consistent Use of Drug Name

- For approved drugs select the generic name and stick with it throughout the form (may use retail name if it is required in the study)
- Investigational drug should also be referenced in the same way throughout the protocol (by a name or a number)

8. Blood Volumes in Lay Friendly Language

- Better in teaspoons or tubes (and not mls.)
- Sometimes confusion around whether the reference is to total blood volume or the amount at each blood draw

8. Blood Volumes in Lay Friendly Language

Examples:	Recommendations:

Study Visit: Cycle 1 Day 1
The following assessments will occur on Cycle 1 Day 1:
• **Vital sign measurements.**
• **Performance status.**
• **Physical exam.**
• **Blood tests,** approximately 103mL of blood will be collected for the following purposes:
  • Routine clinical purposes
  • Research purposes
	Study Visit: Cycle 1 Day 1
	The following assessments will occur on Cycle 1 Day 1:
	• **Vital sign measurements.**
	• **Performance status.**
	• **Physical exam.**
	• **Blood tests,** approximately 7 tablespoons of blood will be collected for the following purposes at this visit:
	  • Routine clinical purposes
	  • Research purposes

9. Formatting Errors, Duplication of Paragraphs

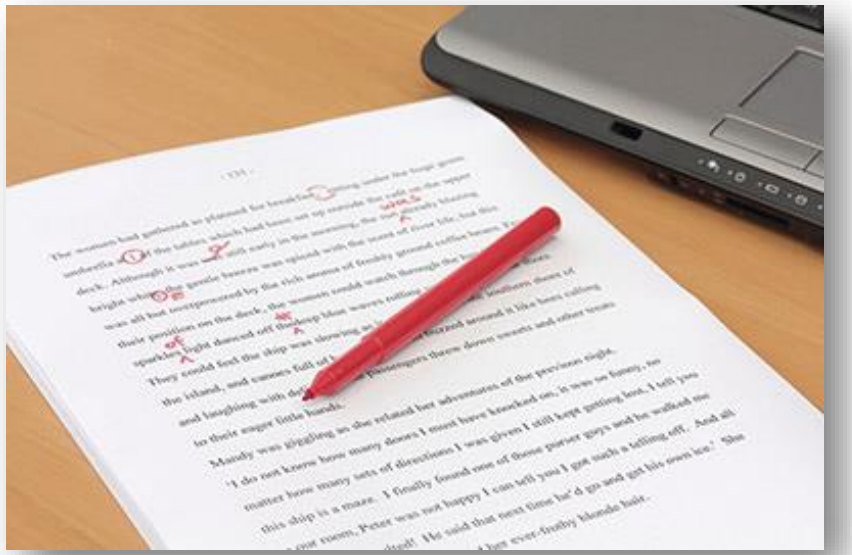
- Consistent Font, Formatting, and typographical errors are in the top ten conditions
  - OHRS Staff fixes minor typos, but often general formatting problems, some paragraphs appear twice, are sent back
- Leave out sections of our template if it does not apply, or is not consistent with what is said elsewhere (e.g. genetic testing)

10. Pregnant Partner Consent is Eliminated

- High frequency of revisions caused delay to new protocol applications
- Will be reviewed when the need arises
- This is preventing 3-4 conditions on each application

Case Study

Review the following paragraph and identify language that would be flagged by the IRB and require revision.



“Your participation will last approximately 52 weeks of study therapy. During the first twelve weeks of the study you will receive AB-120 12.5 mg daily, AV-120 25 mg daily, as well as SOC. Alternatively you may receive placebo. Approximately 33% of patients will receive placebo. The study medication will be taken TID. This is a double-blind study. After receiving the study drug or placebo, 50mL of blood will be collected. You waive any possibility of compensation, including any right to sue, for injuries that I may receive as a result of participation in this research.”

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Key Takeaways

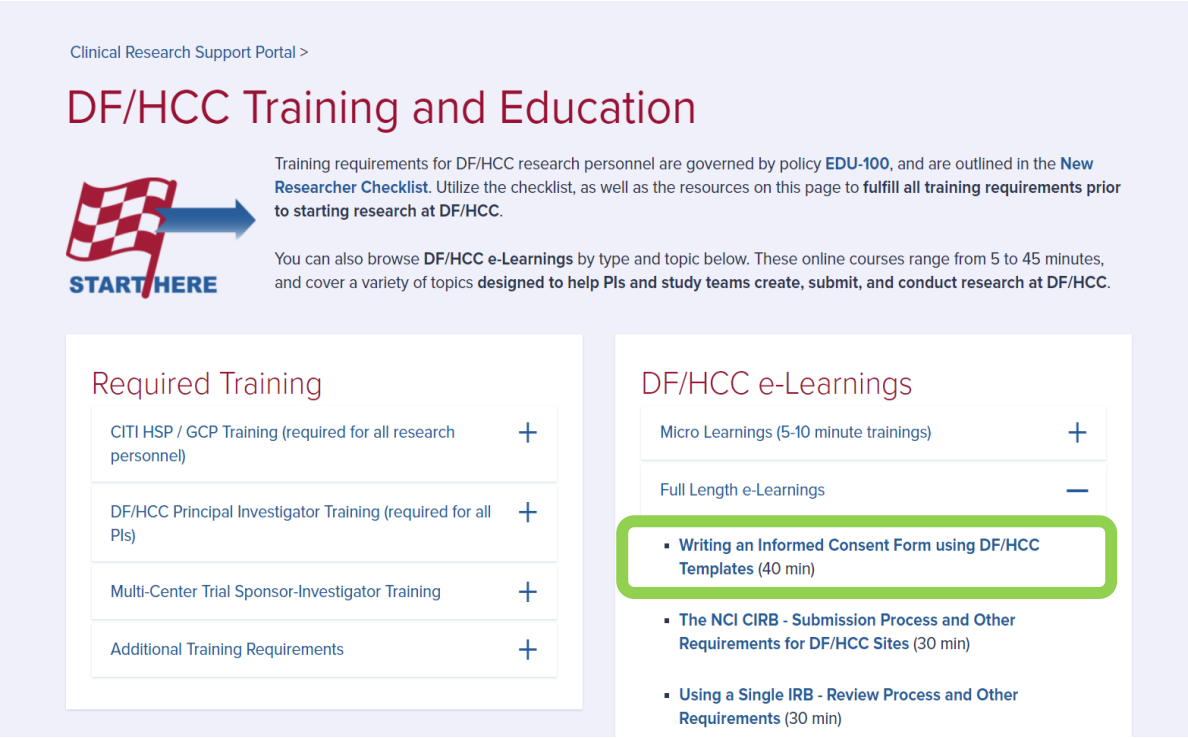
- **Many conditional approvals are due to a few common themes**
  - **Risks** – organize appropriately (by frequency)
  - **Lay language** – avoid technical/overly scientific jargon when describing side effects, etc.
  - **Other common language errors**, e.g., using patient instead of participant/subject, contractual/exculpatory language, inconsistent terms/names
- **Compensation/Remuneration**
  - Include a brief plan for reimbursement, or state that there is none
  - Distinguish between direct payment to participant vs. reimbursement for out-of-pocket costs
- **Pregnant Partner Consents**
  - Should not be submitted to the IRB except when the need specifically arises
- **Use of ICF Template**
  - Be sure to remove sections that don't apply to your study, or that conflict with other sections of the consent

Additional Resources

e-Learning on Writing an ICF using DF/HCC Templates

Detailed step by step guidance and common pitfalls when writing an ICF

https://www.dfhcc.harvard.edu/research/clinical-research-support/clinical-research-support-portal/dfhcc-training-and-education/



Contact OHRS with questions!

OHRS can help with general questions, and provide protocol-specific guidance

OHRS@dfci.harvard.edu