Guidance for Study Teams and Sponsors of Research: Information Regarding Approvable and Not-Approvable Language in Consent Forms

This information sheet provides guidance for study teams and sponsors regarding the language and information that the Dana-Farber Cancer Institute (DFCI) Institutional Review Board (IRB) will permit to be included in the consent form.

Study teams and sponsors are encouraged to adhere to this guidance when drafting consent forms to avoid delays during IRB review. If language that is typically prohibited is necessary for a unique protocol-specific reason, study teams and sponsors should submit supplemental documentation justifying the inclusion of such language.

The DFCI IRB follows the language contained in the Office for Human Research Studies (OHRS) consent document templates.

If an IRB-approved consent document is found to be out of compliance with the guidance provided below and/or the OHRS template, OHRS staff will contact the study team to request changes to the consent form. Submission of an amendment will be required to revise the consent form so that it is brought into compliance with this guidance document and/or the OHRS template consent documents.

Important Note: The expectation is that consent forms are thoroughly proofread and spell-checked prior to submission to OHRS, and that the final draft has been reviewed and approved by the Principal Investigator. The consent document is often a potential participant's first exposure to the study team and it is important that the document reflects the high quality of the research activities conducted at DF/HCC. Extensive issues, including failure to make changes recommended by OHRS staff, will result in an IRB deferral of the submission.

General Information/Guidelines:

- **References to "patients" are not permitted.** Use the word "participants."

- **References to "treatment" are typically not permitted.** FDA and HHS permit the use of "study treatment" but not "treatment" as this implies a clinical course of action.

- **Contractual and potentially exculpatory language is not permitted.** The purpose of the consent is to serve as disclosure tool to subjects regarding the risks and benefits of participation in the research; it is not a contract. The IRB will not approve language that participants may interpret as contractual or that includes legal terminology. Examples of unacceptable language include:
  - "The sponsor has the right to remove you from the study without your agreement..."

- "By signing this consent form, you agree that you forfeit all rights to any inventions..."

- **Template subject injury language may not be altered.** The IRB-approved consent template language regarding participant injury is required. The IRB will not accept language that attempts to limit the sponsor's liability (e.g., "sponsor will not pay for lost wages"), define terms relevant to a legal analysis of liability (including a "research-related injury"), or discuss in detail how coverage may be determined.

- **Technical language is not permitted.** The IRB will not approve language that is overly technical or scientific, or language that is directed towards study teams rather than participants. Please do not copy procedures, including research tables, directly from the protocol. Additionally, all acronyms/abbreviations should be spelled out at first reference.

- **Unnecessary and redundant information is not permitted.** Unnecessary and redundant information adds length to consent forms, distracts from the most important information, and detracts from the informed consent process.

- **Number of patients who have experienced positive or negative results is not permitted.** Information in the consent that states that a specific number of individuals were treated (e.g. 10 participants) with the study treatment previously is irrelevant and would need to be updated when more are treated.

- **References to specific doses of study drugs are not permitted.** The IRB does not permit overly specific information that is subject to change and does not serve to inform participants of what to expect if they enroll.

- **Blood draw measurements are not permitted in milliliters.** Measurements should instead be provided in tablespoons/teaspoons.

- **Instructions and descriptions of "participant responsibilities/requirements" are not permitted.** Instructions and expectations may instead be listed on a participant handout but may not include language such as "you must agree," "participants are required" or other language that may be interpreted as contractual. These information sheets also may not require participant signatures. Examples of unacceptable language include:
  - "You must follow your study doctor's instructions."
  - "You are required to take your oral dose on a full stomach..."

- **Giving participants gift bags, rewards, or other items absent a clinical justification is not permitted.** Providing participants with "swag" incentivizes participants and provides non-clinical motive for participation. Providing such items may also be interpreted as marketing which is not appropriate.

- **Consents which detail multiple cohorts are typically not permitted.** While protocols may involve multiple cohorts, it is often not appropriate to describe all of them in a single consent form. The volume of information may be overwhelming, and it may not be clear for participants to what exactly they are consenting. The IRB suggests breaking the document up into multiple consents so that each consent form is tailored to the

participant's assigned cohort. Another option is to create cohort-specific information sheets or calendars for participants.

- **Reimbursement via pre-paid credit cards cannot be required and must be clearly explained.** The IRB requires that participants be given the option to receive reimbursement via check rather than requiring them to receive pre-paid credit cards. The use of pre-paid credit cards may create an undue burden for participants and unnecessarily provides personal information to third party vendors who may use it for purposes unrelated to the study. If reimbursement via pre-paid credit cards is offered as a reimbursement option, it must be clearly explained to participants what information will be collected and how it will be used.

- **Payment to Study Doctor/Institution:** The IRB will not accept language such as, "The sponsor will pay your study doctor and/or the study site for conducting this study." Such language may imply an improper financial relationship. Please instead include only the DF/HCC template language stating that the sponsor is supporting the research by providing funding, the study drug, etc. If the sponsor/study team believes that there is in fact a financial conflict of interest that should be disclosed to participants, then the details of the conflict must be submitted for review by the IRB.

Common Errors/Oversights Associated with Study Drug Information/Study Treatment Information/Research Results/Future Research Language:

- **Study Drug Mechanism Description:** Oftentimes, the description of how the study agent is intended to work is insufficient. It is either vague or the language is confusing and not lay friendly. The IRB requires a brief explanation of what the study drug is and how it works, using language understandable to the participant.

- **Return of Results:** For language which indicates that individual research results will be returned to the participants, the following is required:
  - Please make sure that the plan for returning results is described in the protocol, and also verify that the results will be obtained or confirmed in a CLIA-certified laboratory.
  - If either of the above cannot be confirmed then the information must be removed from the consent form. The consent may not contain information that is not described in the protocol.

- **Future Research:** The IRB will not require participants to provide samples for unspecified future research as a condition for participation in a treatment study. For any language that refers to "research samples" which appear to be used for future research beyond that required for this study, the following is required:
  - Please make sure that the research objectives for the samples are described in the protocol. If these objectives are not described in the protocol, then they must be removed entirely from the consent form.
  - If the future research objectives for the samples are described in the protocol and will remain in the consent, then they must be described in the optional studies section. In that section, please describe the purposes of the research and what types of analyses will be done. Please ensure that the description is consistent with the plan outlined in the protocol and is written using lay-friendly language.

Please also make it clear that this future research is optional, and include a line for participants to provide or decline consent.

- **Survival Follow Up and Locator Agencies:**
  - The IRB will not approve consent language that states that the study team, sponsor, or third party agencies will review sources such as obituaries in order to determine the status of participants. In order to avoid intrusive, lengthy, and unnecessarily harsh language, only the following statement will be permitted: "We may check publicly available resources for information about you."
  - The IRB will not approve plans for a third party agency to contact participants or their family members/friends. Only members of the study team may contact these individuals. With respect to contacting family members/friends, the consent form must give the participant the opportunity to opt in/opt out (and if opting in, to identify an appropriate contact).

- **Other Treatment Options/Alternatives (Section C of the template):**
  - If applicable, in the standard treatment bullet, please be sure to specify what non-research alternatives may be available to participants.
  - Please also make sure to remove any option that may not be an appropriate alternative for the specific participant population. For example, the bullet point, "Receive the same drugs, but not as part of a research study," would not be a viable option for a first-in-human trial. Similarly, please only include the option of palliative care when appropriate.

Risk Language Guidance:

- **Lay-friendly Risk Language:** Please be sure to describe all risks using concise and lay-friendly language, including a brief explanation of how the participant may be affected by each risk. Where available, please use the language found in the NCCN Consent Language Database (http://www.nccn.org/clinical_trials/informed_consent.aspx)

- **Reversible/Permanent Risks:** For risks such as blindness, deafness, and paralysis, please state whether they are reversible or may be permanent.

- **Serious/Life Threatening Risks:** The OHRS template risk section introduction states generally that risks may be severe and life threatening. The IRB feels this is sufficient information to explain the possible severity of most risks listed in the consent form. Certain risks, however, may require language regarding the specific severity that may be experienced such that including the statement "which may be serious or life-threatening" provides the most accurate information for participants considering the research.

- **Risks Not Specific to Research:** Please be sure to remove any risks that are not specific to the research. For example, please remove the risks of standard of care procedures. Additionally, please remove any risks that are not attributed to the study drug. Only risks that are reasonably foreseeable should be included in the consent form (descriptions of adverse events determined to be unrelated to the study drug are not permitted).

- **Animal Studies References:** Please remove all references to “animal studies” and replace with “laboratory studies” where appropriate. The IRB’s position is that language about animals is unnecessarily descriptive without any benefit as it does not provide clear and meaningful information to participants. Emphasis should be placed on describing the possible risks from the participant’s perspective using lay-friendly language rather than describing the results of particular animal studies. Furthermore, for many studies there is adequate clinical experience with the agent such that references to laboratory findings are not necessary and are potentially confusing.

- **Redundant Risks in Different Categories:** Please make sure that risks are not listed under multiple frequencies. For example, the risk of “fatigue” cannot be listed under both the “Less Common” and “Rare” frequency categories. Please make sure that risks only appear under one category. If similar risks are included, please be sure to clearly differentiate between them.

- **Presentation of Risk Information:** Please present all risks consistently and in bulleted form rather than paragraph form. The IRB’s position is that paragraphs and explanations of risks in narrative form are overwhelming and add unnecessary length to the consent form. Please ensure that the risks are presented clearly, concisely, and consistently. Please also categorize risks by frequency whenever possible.

- **Remove Adverse Event Details:** References to specific numbers of participants that experienced side effects, and details regarding their individual histories and outcomes, are typically not permitted. This information is overly detailed and does not provide meaningful information to participants, and the information is subject to change.

- **Instructions on Contraception:** Please do not add references to birth control methods and proper forms of contraception as this information is overly detailed and instructional. This information may instead be placed on a separate participant information sheet. No participant can be required to use contraception. (Exceptions are permitted for certain drugs with Black Box Warnings such as Lenalidomide and Thalidomide.)