

Standard Operating Procedures for Protocol Submission and Review

1. Purpose

- 1.1. To define the process of protocol review for all clinical research activity under the purview of the Dan L. Duncan Cancer Center.
- 1.2. To assure that cancer related clinical research is undertaken in the most scientifically sound manner, consistent with the guidelines developed for National Cancer Institute designated cancer centers.

2. Scope

- 2.1. This policy applies to all cancer related clinical research within the institutions that comprise the Dan L. Duncan Cancer Center.
- 2.2. All therapeutic and prevention clinical trials whose primary aim is cancer related must receive approval from by the Protocol Review and Monitoring Committee (PRMC) before patient enrollment.

3. Definitions and Abbreviations

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| 3.1. | PRMC | Protocol Review and Monitoring Committee, which is comprised of the Executive Committee and the three working groups |
| 3.2. | BCM | Baylor College of Medicine |
| 3.3. | DLDC | Dan L. Duncan Cancer Center |
| 3.4. | IRB | Institutional Review Board for BCM-affiliated institutions |
| 3.5. | PI | Principal Investigator |
| 3.6. | WG | Working Group of the PRMC |
| 3.7. | EC | Executive Committee of the PRMC |
| 3.8. | AC | Administrative Coordinator |
| 3.9. | NCI | National Cancer Institute |
| 3.10. | RAC | Recombinant DNA Advisory Committee |

4. Materials and Equipment None

5. Protocol Review

5.1. Overview of Review Process

- 5.1.1. All DLDC therapeutic and prevention clinical trials whose primary aim is cancer related must receive approval from by the Protocol Review and Monitoring Committee (PRMC) before patient enrollment.
- 5.1.2. **Subject accrual may not begin until PRMC approval is obtained.**

5.2. Submission for Initial Protocol Review

- 5.2.1. The PI must submit the protocol packet to the appropriate WG (see protocol coversheet, Appendix A, for instructions):

Standard Operating Procedures for Protocol Submission and Review

- 5.2.1.1. **Cell and Gene Therapy (CAGT):** All adult and pediatric protocols that meet one or more of these criteria must go to the CAGT WG:
 - involve the infusion of whole cells or vectors designed to modify the existing genetic structure of cells in subjects
 - target hemopoietic stem cell transplant patients
 - are ancillary to cell or gene therapy studies
 - require RAC review.
 - 5.2.1.2. **Pediatric:** All protocols that target patients less than or equal to the age of 21 and that do not involve cell or gene therapy.
 - 5.2.1.3. **Adult:** All protocols that target patients over the age of 21 and that do not involve cell or gene therapy.
 - 5.2.2. The complete submission packet must include each of these items:
 - 5.2.2.1. **PRMC Initial Review Coversheet** (appendix A), which must be signed by PI or received from PI's institutional email account. The current version of coversheet must be submitted.
 - 5.2.2.2. **Protocol's BRAIN summary report**, as submitted to the IRB (or as to be submitted).
 - 5.2.2.3. **Consent form**, as submitted to the IRB (or as to be submitted).
 - 5.2.2.4. **Full protocol**, as submitted to the IRB (or as to be submitted). In some instances, there will not be a separate protocol document. In such a case, if the protocol components (e.g., procedures, statistics, data review, etc.) are adequately detailed in the BRAIN summary report, then that summary will suffice.
 - 5.2.3. It is highly recommended that the PI submit the protocol to the PRMC before IRB submission.
- 5.3. **Review Path Determination**
- 5.3.1. The WG Chair (or designee) and AC will review the submission to determine whether it has been submitted to the correct WG. If not, the AC will forward to the correct WG and notify the PI.
 - 5.3.2. The WG Chair (or designee) and AC will review the submission to determine whether the protocol requires PRMC review or is exempt.
 - 5.3.2.1. If a submitted protocol is determined to be exempt, the AC will notify the PI that the protocol is exempt from both initial and continuing PRMC review.
 - 5.3.3. If the protocol requires PRMC review, the WG Chair (or designee) and AC will determine whether the protocol qualifies for expedited review (Section 5.4), or requires full review (Sections 5.5 and 5.6).
- 5.4. **Expedited Review**
- 5.4.1. A protocol is eligible for expedited review if it meets one of the following criteria:
 - 5.4.1.1. Approved by the NCI Cancer Therapy Evaluation Program or Cancer Prevention and Control Protocol Review Committee.
 - 5.4.1.2. Supported by an NIH funding mechanism (e.g., R01, U01, U10, P01, etc), which required full peer review as part of the funding process.

Standard Operating Procedures for Protocol Submission and Review

- 5.4.1.3. Is a non-intervention study and is not asking for DLDC support.
 - 5.4.2. The WG Chair (or designee) will perform a review of:
 - 5.4.2.1. Scientific merit
 - 5.4.2.2. Competing studies
 - 5.4.2.3. Prioritization within the DLDC
 - 5.4.3. After this review, the WG Chair (or designee) will forward his/her recommendation to the PRMC Chair (or designee), who will review the recommendation with particular attention to prioritization.
 - 5.4.4. The possible actions during expedited review are the same as for full review (see Section 5.6.4).
 - 5.4.5. The protocol may be re-assigned to the full review path at the discretion of either the WG Chair or the PRMC Chair, if he/she feels that full review is warranted.
 - 5.4.6. The PI will be informed of the PRMC's decision in writing.
 - 5.4.7. Protocol that are approved via the expedited pathway will be added to the agenda and minutes of the next Executive Committee meeting.
- 5.5. **Full Review – Working Group**
- 5.5.1. Once the complete submission packet has been received and the protocol has been assigned to full review, the protocol will be assigned to a WG meeting based on the date the submission was received.
 - 5.5.2. The AC will notify the PI of the WG review date. The PI will be invited to attend that meeting to participate in the discussion of his/her protocol; however, his/her attendance is not required.
 - 5.5.3. The protocol will be assigned a primary reviewer, a secondary reviewer, and a biostatistical reviewer.
 - 5.5.4. The protocol will be distributed to all WG members for their review prior to the meeting.
 - 5.5.5. At the meeting, the WG will discuss the rationale, study design, adequacy of biostatistics, feasibility for completion within a reasonable time frame (particularly with respect to subject accrual), and potential duplication of studies already in progress at DLDC facilities.
 - 5.5.6. During the review, the PI and/or co-investigator(s) may attend the meeting and participate in the discussion at the request of the committee. However, all investigators must leave the room during the final discussion and vote.
 - 5.5.7. The WG may take one of the following actions:
 - 5.5.7.1. Recommend Approval: The WG has no concerns, or previous concerns have been addressed. Protocol will be forwarded to EC with a recommendation for full approval.
 - 5.5.7.2. Approve with Modifications: Protocol requires minor clarifications or a response to concerns, but does not need to be re-reviewed by the full WG. The WG Chair or designee may approve the PI's response, or may request that the full WG review the response at the next meeting.
 - 5.5.7.3. Table: Protocol requires significant modifications and/or the WG has significant concerns. The PI must make the required modifications, and submit the revisions and/or a response to the WG. The response will

Standard Operating Procedures for Protocol Submission and Review

be reviewed at the next WG meeting, and the WG will again vote on the appropriate action.

5.5.7.4. Recommend Disapproval: The WG has serious concerns about the protocol. The protocol will be forwarded to the EC with a recommendation for disapproval.

5.5.8. The PI will be notified of the WG's decision in writing, including any required action or reply.

5.5.9. Once the WG has decided on a recommendation, the protocol will be forwarded for review and final action by the EC (Section 5.6).

5.6. Full Review – Executive Committee

5.6.1. Once the WG has made a recommendation, the protocol will be reviewed at the next EC meeting.

5.6.2. Quorum will consist of 50% of EC members and final outcomes will be determined by majority decision.

5.6.3. The EC will review the protocol and WG correspondence and recommendations. The PI may be invited to the meeting at the EC's discretion.

5.6.4. Possible outcomes include:

5.6.4.1. Approved: Protocol is fully approved. Patient accrual may begin once all other appropriate regulatory approvals are obtained (e.g., IRB, FDA, etc).

5.6.4.2. Approved with Modifications: Protocol requires minor clarifications or a response to concerns, but does not need to be re-reviewed by the full committee. The Chair or designee may approve the response, or may request that the committee review the response at the next meeting.

5.6.4.3. Tabled: Protocol requires significant modifications and/or the EC has significant concerns. The investigator must make the required modifications, and submit the revisions and/or a response. The response will be reviewed at the next committee meeting, and the committee will again vote on the appropriate action.

5.6.4.4. Disapproved: A protocol that is disapproved will not be reconsidered.

5.6.5. The PI will be informed in writing of the committee's decision, including any relevant comments and any required action or reply.

5.7. Exceptions for Pre-Approval Enrollments

5.7.1. In rare instances where a protocol has been approved by the IRB and by the WG, but the EC has not yet reviewed the protocol, the PI may request an exception to enroll no more than three (3) subjects prior to final PRMC approval. Such permission may only be granted with the concurrence of both the WG Chair and PRMC Chair.

5.7.2. The PI must include justification for the exception.

5.7.3. The PI will be notified of the decision in writing.

5.7.4. An exception is not final approval, and the protocol will continue the remainder of its course through the PRMC approval process.

Standard Operating Procedures for Protocol Submission and Review

5.8. Study Prioritization

5.8.1. The PRMC will oversee the prioritization of competing protocols for use of DLDCC resources (e.g., personnel and patients) from all sources, including cooperative group trials and industry trials, thereby ensuring optimal use of clinical resources for scientific purposes.

5.9. Continuing Review

5.9.1. Once a protocol is approved, it will be reviewed by the EC on a periodic basis. The review will occur at least annually; the EC may also decide to conduct review more frequently, e.g., after a certain number of months, or after a certain number of enrollments. The EC will also determine whether amendments to the protocol will be reviewed (see Section 5.10).

5.9.2. It is highly recommended that the PI submit the protocol for PRMC review at the same time as the IRB renewal.

5.9.3. The PI must submit the PRMC Continuing Review Coversheet and the IRB Renewal Report, as per instructions on the coversheet (Appendix B).

5.9.4. Possible outcomes are the same as for initial review (Section 5.6.4). If the PRMC determines that accrual or other aspects of scientific progress are insufficient, the PRMC may take action that it deems appropriate, up to and including requiring that the protocol be permanently closed to subject accrual. The PRMC may also determine that continuing review is no longer necessary.

5.9.5. Continuing reviews will be discussed at the EC meetings, and the discussion and vote will be part of the meeting minutes.

5.9.6. The PI will be notified the committee's decision in writing, including any required action or reply.

5.10. Amendment Review

5.10.1. The PRMC will review all amendments that involve a significant scientific change in the protocol. This includes, but is not limited to:

5.10.1.1. Change in BCM Principal Investigator.

5.10.1.2. Change in or addition of a scientific objective of the study.

5.10.1.3. Change in a BCM initiated study to become multicenter or BCM becomes the coordinating center

5.10.1.4. Addition or deletion of a study arm.

5.10.1.5. Major change in eligibility criteria

5.10.1.6. Addition or deletion of a therapeutic or supportive agent, or major change in administration schedule if the change is due to a change in scientific or safety design.

5.10.1.7. Change in the number of subjects to be accrued if it is due to a change, addition, or deletion of an objective, or due to the results of an interim analysis.

5.10.1.8. Suspension of accrual due to concerns of an IRB or DSMC.

5.10.2. Administrative amendments do not require PRMC review.

5.10.3. Consent form amendments do not require PRMC review, except those resulting from changes outlined in Section 5.10.1.

Standard Operating Procedures for Protocol Submission and Review

5.10.4. Amendments are submitted directly to the EC..

5.11. Record-keeping

5.11.1. The DLDC will maintain central PRMC files for:

5.11.1.1. Completed protocol packets, including the original packet submission, correspondence to the PI, replies/revisions from the PI, and WG and final PRMC approval letters.

5.11.1.2. Minutes from Working Group meetings

5.11.1.3. Minutes from Executive Committee meetings

6. Authority

6.1. **Cancer related clinical protocols may not begin subject accrual until approval by the Protocol Review and Monitoring Committee (PRMC) has been obtained.**

6.2. Authority for DLDC review of clinical cancer related protocols, including initiation, monitoring and termination, has been delegated by the DLDC Director to reside with the PRMC. The DLDC Director is informed of all approval and termination actions.

7. References

7.1. These procedures were developed in accordance with the NCI guidelines for protocol review and monitoring, as required for all NCI cancer centers.