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AE	Adverse Event
BCM	Baylor College of Medicine
CAGT	Cell and Gene Therapy
CTEP	Cancer Therapy and Evaluation Program
CTSU	Clinical Trial Support Unit
DLDCCC	Dan L Duncan Comprehensive Cancer Center
DCTD	Division of Cancer Treatment and Diagnosis
DRC	Data Review Committee
DSMB	Data and Safety Monitoring Board
DSMP	Data and Safety Monitoring Plan
FDA	Food and Drug Administration
IRB	Investigational Review Board
NCI	National Cancer Institute
NCTN	NCI National Clinical Trials Network

[redacted]

As an NCI-designated cancer center, the Dan L. Duncan

Officer (PSO). The structure and scope of responsibility for these committees as well as the role and responsibilities of the PSO are described below. The committees and the PSO report to the Clinical Research Leadership Committee (CRLC) within the DLDCCC and ultimately to the Cancer Center Director. The oversight structure is outlined in Figure 1 below.

The DLDCCC Data and Safety Monitoring Plan has been developed to coordinate data and safety monitoring oversight for all cancer clinical trials consistent with the following policy statements:

- National Institutes of Health Policy for Data and Safety Monitoring
  (10-Jun-98) http://grants.nih.gov/grants/guide/notice-files/not98-084.html
  (05-Jun-00) http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html
- National Cancer Institute policy for data and safety monitoring of clinical trials
  http://deainfo.nci.nih.gov/grantspolicies/datasafety.pdf
- Cancer Therapy Evaluation Program (CTEP) guidelines for monitoring of clinical trials for

The Clinical Research Leadership Committee (CRLC), composed of DLDCCC senior leadership, reviews reports from the Data Review Committee (DRC), Data and Safety Monitoring Boards (DSMBs), and QA/QC audits, which are independently submitted to this committee. This committee is comprised of the DLDCCC Director, the Associate Directors for Clinical Research, the Associate Directors of the CTSU, the Chair and Vice-Chairs of the Executive Committee, the Chair(s) of the DRC, and the Director of the Quality Shared Resource. The Data Review Committee and Data Safety DLDCCC investigator-initiated protocols report to the CRLC is provided as an appendix to the DSM Plan.

the DLDCCC. All activities involving human subjects must be reviewed and approved by the IRB of record prior to patient enrollment. Data Review Committee Reports and Data Safety Monitoring Reports are provided to the investigator who is responsible for providing these

Information related to any study under DLDCCC review, including study data, reports, correspondence, and appeals, will be maintained as confidential and disclosed only as required for review, unless additional disclosure is required by BCM policy or pertinent laws or regulations. All members of the review committees are subject to BCM and federal confidentiality requirements. Members will be reminded upon their appointment to committees and regularly throughout their committee service.

The clinical research infrastructure of the DLDCCC includes a Patient Safety Officer (PSO) who ensures that all data monitoring for Cancer Center trials is conducted in accordance with the approved monitoring plan. The PSO reports to the Associate Directors of Clinical Research.

Responsibilities of the PSO include the following:

- Maintenance of a database that tracks protocol reviews and approvals
- Monitoring adherence to the study's approved DSMP
- Notification of the Associate Directors for Clinical Research and the CLRC if a plan is not being followed appropriately
- Advising clinical trial investigators regarding the optimal data and safety monitoring plan during development of investigator-initiated trials
- Coordinating the DLDCCC DRC (including maintaining member roster, coordinating meetings, sending/receiving correspondence, etc.)
- Facilitating the development of independent DLDCCC-coordinated Data and Safety Monitoring Boards (including constituting the DSMB, coordinating meetings, sending/receiving correspondence), as required.

The purpose of the Protocol Review and Monitoring System is to provide internal, centralized oversight of cancer clinical research within the DLDCCC. The Protocol Review and Monitoring Committee (PRMC) reviews interventional clinical trials whose piaw a

- addition or deletion of an arm of the study;
- major change in eligibility criteria;
- addition or deletion of a therapeutic or supportive agent, or major change in schedule of administration if the change is due to a change in scientific or safety design;
- 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;
- change in the protocol in response to suspension of accrual due to concerns of an IRB or DSMC/DRC/DSMB.

Amendments for studies which undergo expedited review (such as NCTN trials) are not reviewed by the PRMC.

At the time of each protocol's annual IRB review, the PRMC Executive Committee conducts a full review of each open-to-accrual protocol to ensure that reasonable progress is being made; however, review may be conducted more frequently at the discretion of the Committee.

Further details about the PRMC process can be found in the PRMC Standard Operating Procedures (SOP), which are available to Investigators and PRMC members on the DLDCCC website (https://www.bcm.edu/centers/cancer-

Each DLDCCC protocol must have a data and safety monitoring plan that is reviewed and approved by the PRM545.16Tappr52 mR

related to the study should be reported to the review committee (DRC or DSMB) within 15 calendar days of knowledge of event.

- For studies in which the IND is held by a DLDCCC investigator, any event that is reported to the FDA should also be reported to the DRC/DSMB at the same time.

The DLDCCC has an established Data Review Committee (DRC) that performs data and safety monitoring activities for all DLDCCC investigator-initiated clinical trials that do not require full independent DSMBs. The DRC has a broad membership which covers a range of expertise and specialties. The DRC convenes at least once per month.

The DRC Chair is appointed by the DLDCCC Director, in consultation with the Associate

High risk studies may also be assigned a first-enrollment audit to be conducted by the QA program.

The minimum level of monitoring required for investigator-initiated trials is a DRC review on an annual basis. More frequent review may be required based on risk of the intervention. Also, additional monitoring may be required based on the findings of the initial review.

DRC review should continue until all subjects have completed study-related interventions, unless determined otherwise by the DRC.

If the DRC finds a study report to be unsatisfactory, the report may be returned for revision while the study continues, or the study may be paused until all questions are answered to the committee's satisfaction. The DRC may require more frequent reports from the study team or request an audit of the study. The DRC may also recommend protocol closure if there are safety concerns or if a study fails to accrue in a manner which will allow the scientific question to be addressed.

Review of studies by the DRC includes two parts. The first part is an open session in which members of the study team may be present to answer questions posed by the DRC. Following the open session, there is a closed session in which members of the study team, as well as any DRC member who has an indirect or direct relationship with the study under review, are recused from the discussion in order to eliminate any conflict of interest. During the closed discussion, the DRC discusses interim outcome results, decides what actions are to be taken, and votes.

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In the unlikely situation that the trial PI does not concur with a DRC recommendation for modifying or halting a study, he/she may formally appeal the DRC's decision. The PI must inform the DRC in writing of the reason(s) for disagreement and any alternate proposal. The DRC will meet to review the appeal. The DRC may vote to accept or reject

Each DSMB will have at least 5 members, including a statistician who is not associated with the study.

- For study-specific DSMBs, the study PI will suggest external members with appropriate expertise to interpret the data and ensure patient safety. Investigators directly involved with the conceptual design, conduct or analysis of the particular trial are not eligible to serve on the DSMB.
- For the standing DLDCCC External DSMB, membership will be selected by DLDCCC Clinical Research Leadership; no member may have a current affiliation with the DLDCCC or BCM.

The Patient Safety Officer is a non-voting member and will coordinate the establishment and operational aspects of the DSMB.

DSMB responsibilities include issues related to patient safety (specifically adverse events and the risk/benefit ratio of the trial), and interim analyses and study conduct necessary to accomplish the primary protocol objectives (including patient accrual, adherence to the study design, outcome measures, and release of protocol-related primary outcome data). The DSMB is expected to explicitly recommend closure, revision, or continuation each time the protocol is reviewed.

Each DSMB is charged with providing oversight of study progress and will review the same information reviewed by the DRC, as discussed above. The DSMB may choose to review other aspects of the study, and those aspects will be outlined in the DSMB charter.

Each DSMB will determine the schedule for review of the data based on the study's risk level, size, and complexity. The DSMB may elect to conduct a review at regular time periods (e.g., every 6 months) or after a certain number of patients are enrolled. The DSMB must review the study at least annually. For internally initiated, non-IND studies, DSM should continue until all subjects have completed protocol interventions and procedures. For internally initiated, IND studies, DSM of studies should continue until the IND is closed, or until the DSMB determines that review is no longer needed. At time of study closure, a final report and notice of the closure should be sent to the CRLC.

A statement that the protocol has been reviewed by the DSMB will be submitted to the PI for submission to the IRB and Federal funding/oversight agencies (as applicable). If study changes are recommended by the DSMB, it is the responsibility of the PI to implement these changes (through the IRB and other appropriate regulatory agencies) and notify the DSMB after the changes have been made. Failure to implement modifications recommended by the DSMB prior to timeframe required by the DSMB can result in the study being halted by the DLDCCC Director.

The DLDCCC CRLC will be informed of DSMB reviews and determinations.

In the unlikely situation that the trial PI does not concur with a DSMB determination for modifying or halting a study, he/she may formally appeal the DSMB's decision. The PI must inform the DSMB in writing of the reason(s) for disagreement and any alternate proposal. The DSMB will meet to review the appeal. The DSMB may vote to accept or reject the appeal. If the appeal is tent aj.6 (m)4.2 (t)-6-6.6 (ony)8.9 (0.6 (he/)-16 (he)0.6 (D)2.5 (ac)-P

assessment at protocol defined intervals.

Reports will be submitted to the DRC at the frequency outlined in the protocol's approved DSMP.

In particular, the study PI must notify the DRC when a study transitions from Phase I to Phase II and must notify the DRC if additional cohorts are opened or added.

All phase III trials and some phase II trials with a placebo control will have a DSMB constituted and functioning as described above.

These trials are usually low risk and pose no more than minimal risk to the participant. Monitoring will be commensurate with risk and must be outlined in the protocol's DSMP.

The PI is responsible for the accurate, appropriate, and timely reporting of all necessary adverse events (AEs) to the IRB of record, the sponsor, regulatory agencies, participating institutions, and co-investigators as outlined in the protocol.

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within 15 calendar days of knowledge of event.

- For studies in which the IND is held by a DLDCCC investigator, any event that is reported to the FDA should also be reported to the DRC/DSMB at the same time.

Adverse events that are reported should be sent the DLDCCC Patient Safety Officer (PSO) by the PI and study team. The PSO will review and distribute the report to the DRC/DSMB Chairs and members and send any correspondence back to the PI.

For DLDCCC investigator-initiated multi-center trials in which a DLDCCC site is the coordinating center, each participating institution must submit AEs to the DLDCCC PI cl w 0 0 apf12 -0 0 T

on investigator-initiated trials and other high-risk trials