Fred & Pamela Buffett Cancer Center

Institutional Data and Safety Monitoring Plan

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DATA AND SAFETY MONITORING PLAN

The University of Nebraska Medical Center (UNMC) Fred & Pamela Buffett Cancer Center (BCC) data and safety monitoring plan is designed to ensure the safety of participants in clinical trials conducted by BCC members and to comply with National Cancer Institute (NCI) and National Institutes of Health (NIH) requirements. This document covers monitoring procedures for all BCC investigator-initiated institutional trials, including multi-center investigator-initiated institutional trials regardless of whether BCC is the lead institution. Primary responsibility for monitoring industry, other externally peer reviewed and cooperative group trials belongs to the sponsor and cooperative group, respectively. As outlined below, the results of these external monitoring procedures are reported to the BCC Data and Safety Monitoring Committee (DSMC), Scientific Review Committee (SRC), Audit Committee (AC) and Associate Director for Clinical Research.

I. Overview of the Organization of Responsibilities for Scientific Review and Data and Safety Monitoring

Ensuring subject safety and scientific integrity is ultimately the responsibility of the BCC Director, Dr. Kenneth Cowan, and the Associate Director for Clinical Research, Dr. Apar Ganti. To assist with this responsibility, three BCC committees exist. Each committee reports to the Associate Director for Clinical Research (except when he/she is Principal Investigator (PI) of a protocol, In these cases, the committees report their findings directly to the BCC Director.) The committees and their interrelationships are described below.

A. Scientific Review Committee (SRC) (see Appendix 1 for membership)

The SRC is responsible for initial scientific review of protocols requiring informed consent and addressing a cancer-related question. The SRC also reviews all changes or amendments to previously reviewed protocols and reviews study progress at least annually. The progress review includes: (1) the percentage of accrual goal reached to date; (2) major developments making the scientific question more or less important or may indicate the study's objective cannot be met; and (3) any competing protocols for prioritization.

The SRC meets monthly and the review results are provided to the protocol's PI. A protocol cannot open to accrual until approved by the SRC, by the DSMC where required, and by the UNMC/Nebraska Medical Center (NMC) Institutional Review Board (IRB.) The SRC is also responsible for the ongoing annual scientific review of BCC protocols. The SRC receives reports from the DSMC, which is responsible for the ongoing monitoring of adverse events and from the AC, which is responsible for ensuring protocol compliance. The SRC actions are reported to the protocol's PI, the AC, the DSMC, the IRB and the Associate Director for Clinical Research.

B. Data and Safety Monitoring Committee (DSMC) (see Appendix 2 for membership)

The DSMC consists of at least 6 members: four BCC members actively involved in clinical research, a biostatistician, and a patient advocate. It is responsible for monitoring all BCC investigator-initiated intervention trials to ensure subject safety. The DSMC meets monthly to review detailed reports of all serious events and the cumulative toxicity experience of all subjects enrolled on those studies falling within its purview, as well as interim analysis and dose cohort changes for these studies. The DSMC reports its actions to the protocol's PI, the SRC, the AC, the IRB and the Associate Director for Clinical Research.

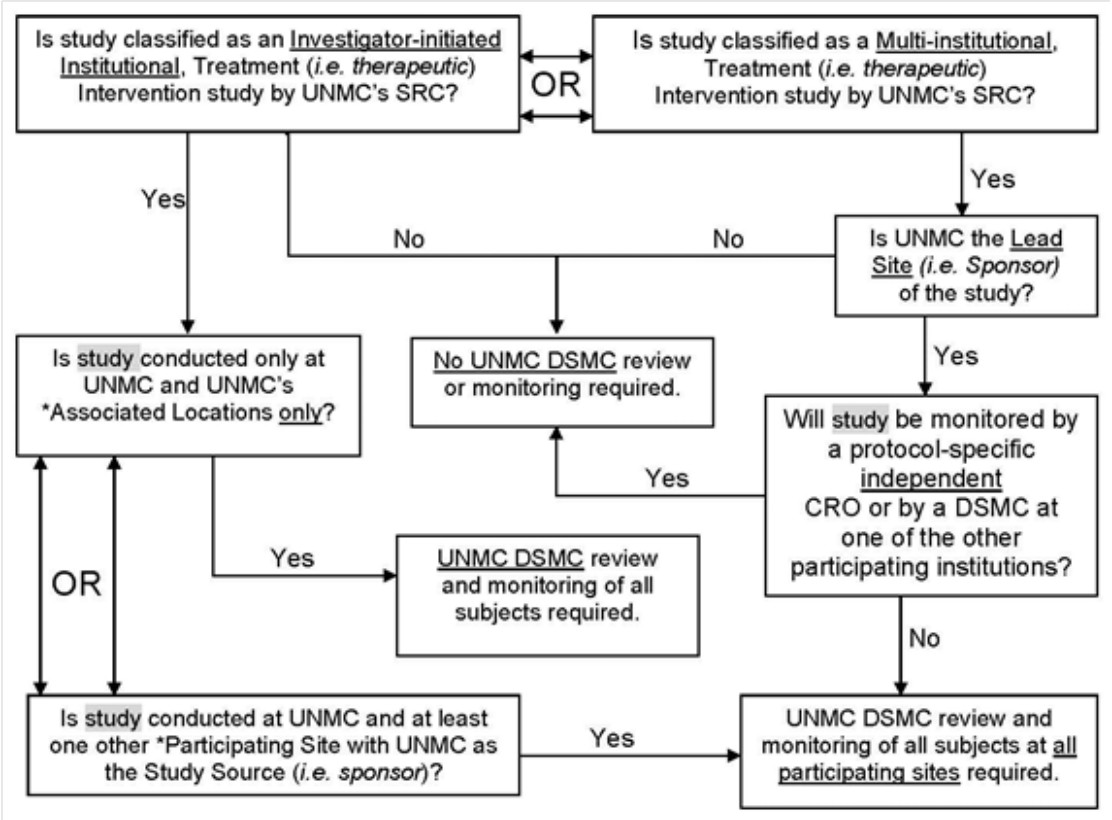
C. Audit Committee (AC) (see Appendix 3 for membership)

The AC consists of four (minimum) BCC members, including at least one physician. Audits are conducted by the Protocol Review and Monitoring System (PRMS) Administrator and/or Auditor and reported to the committee during a monthly meeting. The committee audits intervention cancer protocols not monitored by an external body, such as the industrial sponsor or, in the case of NCI-funded cooperative group trials, the Group or Theradex, Inc. The committee ensures protocol compliance by reviewing the adequacy of informed consent, enrollment of appropriate subjects, implementation of protocol-specified procedures and treatment, adequacy of data collection, and appropriateness of adverse event monitoring and reporting. The Audit Committee reports its findings to the protocol's PI, to the SRC, to the DSMC, to the IRB and to the Associate Director for Clinical Research.

D. Committee Structure and Relationships

E. Protocols Requiring DSMC Review

All cancer-related protocols involving human subjects classified as investigator-initiated intervention trials by the BCC's SRC require review by the DSMC prior to activation of enrollment. Protocols designated as minimal risk to the study subjects may be exempted from DSMC review. All protocols designated as interventional treatment trials will be subject to DSMC oversight. Study investigators may choose to establish a separate study-specific DSMC, subject to the approval of the UNMC DSMC. To be classified as an investigator-initiated interventional trial, the protocol must be designed and developed by a PI who is a BCC member and be a clinical trial with a primary purpose of treatment intent using an agent or device (e.g. device, drugs, radiation, surgery, and/or biological agents). This includes investigator-initiated, multi-site trials and investigator-initiated trials (single or multi-Site) sponsored by UNMC, but coordinated by either UNMC or an external agency.



II. Identification and Management of Potential Conflicts of Interest of DSMC Members, DSMC Consultants and PRMS Staff

The DSMC policy requires all potential financial and non-financial conflicts of interest of DSMC members, DSMC Consultants, and PRMS staff must be self-identified to the best of the individual's knowledge and appropriately managed to prevent such conflicts from interfering with the objectivity and validity of the DSMC review and monitoring process. The DSMC does not require disclosure of the nature of the conflict unless an exception is requested (see Section II.B.6).

A. Definitions

1. **Covered Persons**
   Covered persons include DSMC members, DSMC Consultants, and PRMS staff. Financial interest accruing to immediate family members of a Covered Person (spouse, dependent children, parents or anyone a Covered Person may claim as a dependent under the Internal Revenue Code) are considered as a financial interest of the Covered Person.

2. **Potential Conflicts of Interest**
   The following are financial and non-financial conflicts of interest that exclude DSMC members and DSMC Consultants from participating in the DSMC protocol and adverse event review process. PRMS staff who have any of the conflicts listed below are excluded from serving as the key PRMS administrator assigned to the study in question.
   a. The Covered Person serves as a PI or Secondary Investigator (SI) and is, accordingly, listed on the DSMC research protocol or adverse event submitted for review.
   b. The Covered Person is an advisor, or a direct supervisor, of a trainee (e.g., medical, graduate or undergraduate student) who is PI or SI and is listed on the DSMC research protocol or adverse event submitted for review.
   c. The Covered Person has a financial interest defined as: (1) salary, royalties or a commitment for future royalties, consulting fees, honoraria, gifts, or other payments received in the last 12 months, will be received while the research is being conducted or will be received within 12 months after the research is completed; or (2) an equity interest in the sponsor of the research. Mutual funds are excluded.
   d. The Covered Person holds a significant position such as director, officer, partner, or trustee in the company sponsoring the research or has held such a position in the past 12 months.
   e. The Covered Person holds patent rights or royalties from such rights whose value may be affected by the outcome of the research, including royalties under any royalty-sharing agreements involving UNMC, the Nebraska Medical Center, UNeMed
   f. The Covered Person has a financial interest in a company with a marketed product or is in the process of developing a new product which is, or will be, in direct market competition with the product; or is potentially related to a direct market competitor of a product in the research protocol or adverse event submitted for DSMC review.
   g. The Covered Person has a personal relationship, or conflict, with any research personnel listed on the research protocol which would potentially cause the DSMC member, in his/her opinion, to be less than objective in his/her review.
   h. The Covered Person does not have a conflict of interest if he/she serves on the sponsor's scientific advisory board for an area unrelated to the research under review.
   i. If a Covered Person is listed on the research protocol as a participating physician or other study personnel, he/she does not have a conflict of interest providing his/her only involvement in the protocol is in the context of providing clinical care to subjects and there is no expectation the Covered Person will be included as an author on any papers resulting from the research.
   j. If a Covered Person is listed on the research protocol as a participating physician involved in obtaining and documenting informed consent as well as providing clinical care, the individual may serve as a DSMC reviewer and participate in the discussion. However, such DSMC member reviewers, however, must abstain from voting.
   k. If a Covered Person perceives a conflict of interest not otherwise listed above.

B. <u>Procedures for Identification and Management of Conflict of Interest</u>

1. All DSMC members must notify the DSMC Chair or designee of a potential conflict of interest within three days of receiving notification of assignment as a reviewer. If the DSMC member is uncertain a potential conflict of interest exists, they are encouraged to consult with the DSMC Chair or designee.

2. Whenever a prospective consultant is asked to review a protocol, he/she is provided a copy of the DSMC Conflict of Interest Policy and will be excluded from serving as a consultant if a conflict exists. Consultants must certify in writing they do not have a conflict of interest.

3. Prior to the beginning of each meeting, DSMC members are asked to declare the existence of any undisclosed conflicts, but are not required to describe the nature of the conflict.

4. All PRMS staff must immediately notify the DSMC Chair or designee of any existing conflict. The DSMC Chair or designee will determine any necessary action.

5. When the DSMC member has a conflict of interest, he/she may not participate in the discussion and voting of the review of the protocol in question. The DSMC member may not vote on any protocol where he/she has a conflict of interest as defined above. Upon request of the DSMC, the member may provide information or respond to questions.

6. If a DSMC member has a conflict of interest as defined by Section II.A of this policy, but in his/her opinion, the conflict will not interfere with the objectivity and validity of the review, the member may request an exception allowing the member to serve as a reviewer and be granted voting privileges. In such cases, the following procedure must be followed:
   a. The DSMC member must disclose the specifics of the conflict to the DSMC Chair/designee.
   b. The DSMC member must indicate whether they wish to serve as follows: (1) assignment as a reviewer with or without voting privileges; or (2) no assignment as a reviewer, but with voting privileges.
   c. The DSMC Chair will review the conflict and determine whether the exception is granted.
   d. The full DSMC is notified of any exception and may request further details. The full DSMC has the authority to overturn approval of an exception.

C. The name of the DSMC member with a conflict of interest, prohibited by policy from participating in the discussion and is not permitted to vote, will be included in the meeting minutes.

III. Data and Safety Monitoring Procedures

A. Confidentiality of Data

All reports submitted to the DSMC for review are first "blinded" by removing all subject identification information. Information regarding an individual subject's assignment to arms of randomized and blinded studies is not routinely provided to the DSMC. However, in order to complete the DSMC review, the DSMC may request unblinding of the subject's treatment assignments.

B. Monitoring the Progress of Trials and the Safety of Participants

Trials conducted by BCC members are monitored by the DSMC for safety, the SRC for scientific integrity and study progress, by the AC for protocol compliance, and by the institution's IRB. The DSMC assigns the frequency of data and patient safety monitoring according to the type of trial and the potential risks.

For all BCC studies, the PI is required to report adverse events to the BCC's PRMS Office and to the IRB as specified in Section 9.0 of the BCC's structured protocol document (or the equivalent adverse event reporting section of a cooperative group or industry-sponsored protocol document). The PRMS office will confirm all agency notifications required by protocol have been submitted. The DSMC Chair will determine the need for an immediate full DSMC review or whether it can be reviewed at a regularly scheduled DSMC review of the protocol (see below for the protocol-specific schedule for regular DSMC reviews).

C. Level of DSMC Review of Investigator-initiated Institutional Protocol Research

For all protocols under DSMC review, the DSMC assures the protocol instructions for reporting of adverse events to the BCC's PRMS Office and the IRB as outlined in the protocol document are consistent with the protocol-specific subject risk, and with all federal adverse event reporting requirements.

1. **Non-therapeutic trials and other trials without significant health and safety risk:** These trials include studies involving routine blood or tissue sampling, survey research, questionnaires, observational studies (involving data collection, but no interventions beyond routine patient care). Protocols classified by the SRC in this category will be **exempt** from routine DSMC review.
2. **CTEP-sponsored cooperative group studies:** Protocols classified by the SRC in this category will be **exempt** from routine DSMC review because they receive ongoing adverse event monitoring by the cooperative group and annual review of toxicity by the IRB.

3. **Industry-sponsored studies for which UNMC participates**: Protocols classified by the SRC in this category will be **exempt** from routine DSMC review, secondary to ongoing adverse event monitoring by the sponsor and annual review of toxicity by the IRB.
4. **Institutional Prevention and Cancer Control Intervention studies:** These trials include limited intervention studies without significant risk Protocols classified by the SRC in this category will be reviewed by the DSMC prior to activation of enrollment. If these protocols are determined to present minimal risk to study subjects, they may be designated as **exempt** from further DSMC review and DSMC review of adverse events experienced on these trials will not be required. All studies presenting more than minimal risk will be subject to DSMC review, although investigators may choose to establish a separate study-specific DSMC, with the approval of the DSMC.
5. **Institutional Phase I studies:** PIs will conduct continuous review of data and subject safety. Institutional Phase I studies are reviewed at minimum quarterly by the DSMC.
6. **Institutional Phase II and Pilot Studies:** PIs will conduct routine reviews of data and subject safety. Institutional Phase II and Pilot studies are reviewed at minimum semiannually by the DSMC.
7. **Institutional Multi-site trials conducted at affiliate sites and Multi-center trials conducted at participating sites with UNMC as the sponsor:** Protocols initiated by a UNMC Investigator with participation by multiple institutions must be monitored by the DSMC or a board specifically designed for the individual study. The frequency of monitoring is determined by trial type and potential risks. The DSMC Policies and Procedures for monitoring multi-site and multi-center institutional trails are outlined in Appendix 4.

The results of the DSMC review of protocol adverse event summaries, of serious adverse events and of a newly submitted protocol's plan for adverse event monitoring and reporting will be communicated in writing to the PI, the SRC, and the Associate Director of Clinical Research. Full SRC approval of newly submitted protocols *will not* be granted until the DSMC's recommendations for changes have been satisfied. The DSMC will forward its recommendations regarding changes to the protocol or protocol conduct to the SRC and IRB.

PI compliance with protocol requirements regarding the reporting of adverse events is tracked by the PRMS Administrator and reported to the DSMC. Compliance is also assured through the Audit Committee process (see Section V.C below).

IV. Review of New Protocols, Changes to Protocol and Adverse Events

A. DSMC Review of New Protocol Submissions

New cancer-related protocols are submitted to the SRC for review, as outlined in the SRC policies and procedures. The PRMS Office forwards protocols requiring monitoring by the DSMC, to the DSMC for initial review.

The DSMC reviews the protocol, focusing on the section pertaining to Adverse Event Reporting Guidelines and Toxicity. The DSMC communicates recommendations regarding changes to the protocol or protocol conduct to the PI in writing. The DSMC also reports these recommendations to the SRC Chair, and the SRC will incorporate these recommendations into the SRC review process.

B. DSMC Review of Changes to the Protocol's AE Reporting Guidelines

Significant changes made to previously reviewed paragraphs pertaining to Adverse Event Reporting Guidelines and Toxicity in protocols reviewed and monitored by the DSMC, require review and approval as outlined in Section IV.B. If immediate changes are required to protect the safety of research subjects, the DSMC chair may grant conditional approval of such changes pending review of the proposed changes by the full DSMC.

C. Focus of DSMC Review

During initial protocol review or review of significant changes to the section pertaining to Adverse Event Reporting Guidelines and Toxicity reviewers will focus attention on whether the protocol contains:

1. A clear and unambiguous definition of the instrument used to grade Adverse Events (CTCAE v. 5.0 recommended, but alternatives are acceptable as long as they are clearly defined).
2. A clear and unambiguous definition of Adverse Events.
3. A clear and unambiguous description of all Adverse Events reportable to the DSMC. The DSMC requires all AE's Grade 3 or higher (using CTCAE v. 5.0), expected or unexpected and regardless of attribution, to be reported. The DSMC recognizes certain toxicities are routinely anticipated on certain protocols (e.g. Grade 4 hematologic toxicity on transplant protocols, etc.). The investigator may specify in the protocol that a particular toxicity is anticipated for the vast majority of research subjects and such toxicity will not be reported. The DSMC will determine in its initial review of the protocol if such exclusion from standard reporting guidelines is acceptable.
4. A clear and unambiguous description of dose escalation and de-escalation criteria used, including a clear definition of dose limiting toxicity, where relevant.
5. Stopping rules for excessive toxicity and/or lack of efficacy where relevant.
6. A need for interim analysis.

D. Frequency of Monitoring

In its initial review, the DSMC will make a recommendation for the frequency of DSMC monitoring based on an assessment of risk associated with protocol therapy:

- Quarterly review, if the risk for protocol associated adverse events is considered significant
- Semi-annual review if the risk for protocol-associated adverse events is considered low
- Annual review if the risk for protocol associated adverse events is considered very low

The frequency of monitoring may be changed based on the frequency or severity of adverse events encountered. A change in the frequency of monitoring is communicated to the protocol's PI in writing.

E. Scheduled Review of Cumulative Adverse Events

The level of scheduled review of cumulative internal AEs by the DSMC reflects the level of risk associated with the protocol. During the review, the DSMC will focus on the frequency and severity of expected adverse events, the occurrence of unexpected adverse events, and the correct attribution of all reported adverse events.

A protocol specific DSMC submission form (see pages 23 - 29) must be submitted to the DSMC upon notification of a scheduled AE review. This report must be accompanied by a hard copy of the DSMC AE Reporting Worksheet (see pages 32 - 33) summarizing all grade 3 or higher internal AEs (including SAEs that have been fully reported and reviewed by the DSMC). The AE Reporting Worksheet must also be submitted electronically and sorted by AE to the BCC PRMS Administrator. Electronic forms are available on the PRMS website at http://www.unmc.edu/cancercenter/clinical/prms.html.

Results of the DSMC review of the Data and Safety Monitoring Report and the AE Worksheet will be communicated in writing to the PI, the SRC, the Associate Director of Clinical Research and the IRB.

F. Reporting Serious Adverse Events

Any Internal AE that meets one or more of the definitions of SAE outlined in Section IV.G and/or meets the UNMC IRB requirements for reporting must be fully reported to the DSMC. The PI is responsible for submitting a copy of the IRB's Internal AE or Fatal AE (FE) Report Form along with a blinded copy of any related patient source documents to the DSMC.

SAEs should be fully reported to the DSMC when they are reported to the IRB. Reporting of SAEs to the DSMC is expected within seven business days of the occurrence of the event. If additional information about the SAE is pending, a preliminary report should be filed within seven (7) business

days with final reporting when additional information is available. Failure to report an SAE as required is considered a protocol violation and may be reported to the Associate Director for Clinical Research.

G. Definition of a Serious Adverse Event

An Internal Adverse Event is serious and should be fully reported when the patient outcome is:

1. **Death**: Any death occurring while the subject is being treated on protocol or occurs within 30 days of completing research related interventions.
2. **Life-Threatening**: When the subject was at substantial risk of dying at the time of the adverse event or it is suspected the use or continued use of the study drug or device would result in the subject's death.
3. **Hospitalization (initial or prolonged):** An admission to the hospital or prolongation of a hospital stay that is the result of an adverse event.
4. **Disability**: If the adverse event resulted in a significant, persistent, or permanent change, impairment, damage, or disruptions in the patient's body function/structure, physical activities or quality of life.
5. **Congenital Anomaly:** If there are suspicions that exposure to a medical product prior to conception or during pregnancy resulted in an adverse outcome in the child.
6. **Requires Intervention to Prevent Permanent Impairment or Damage:** If it is suspected that the use of a medical product may result in a condition which required medical or surgical intervention to preclude permanent impairment or damage to a patient.

H. Review of Dose Cohort Changes on Phase I Trials

While no DSMC approval is required before the PI decides to change a protocol's dose level either up or down, the PI must notify the DSMC upon doing so by completing the Dose Level Change Report (see page 30 - 31) and submitting it for review at the next regularly scheduled DSMC meeting.

I. Review of Interim Analyses

Protocols monitored by the DSMC may contain stopping rules for excessive toxicity or lack of efficacy. Whenever an interim analysis is performed to ensure no protocol defined stopping rules have been met, a copy of the analysis must be forwarded to the DSMC. The DSMC will acknowledge the receipt of the analysis and discuss the results at its next regularly scheduled meeting.

V. Reporting Relationships and Procedures for Reporting Results of DSMC Review

The DSMC will communicate the results of all reviews and its recommendations regarding changes to the protocol or protocol conduct to the PI in writing. Written communications to the PI are signed by the DSMC Chair, unless the Chair is a named investigator on the protocol being reviewed. In this case, a member of the DSMC Committee will sign. The DSMC also reports its recommendations to the SRC Chair, and the SRC incorporates these recommendations into the SRC review process. To decrease the submission burden for investigators, initial review of protocols is coordinated with the initial review by the SRC.

The DSMC reports to the BCC's Associate Director for Clinical Research. Minutes from the DSMC meetings are also submitted to the SRC, the Audit Committee and the IRB, for informational purposes.

Plans to Assure Compliance

A. Plans for Assuring Compliance with Requirements Regarding the Reporting of Adverse Events

Section 9.0 of each BCC protocol specifies the toxicity reporting guidelines. These adverse event (AE) reporting guidelines conform to the reporting requirements outlined in Tables 1 through 5. For investigator-initiated protocols, the DSMC will assure that the protocol instructions concerning the reporting of AEs to the BCC's Protocol Review and Monitoring Office (PRMS) and the IRB (section of the SRC template) are consistent with the protocol-specific subject risk, and with all federal AE reporting requirements. The DSMC will require changes to protocols in cases judged inadequate.

All protocol specified AEs from investigator-initiated Pilot, Phase I, Phase II, and Phase III studies are reported on standard Adverse Event Reporting Worksheet directly to the BCC's PRMS Office and separately to the IRB. Adverse event reporting for (1) non-therapeutic trials and other trials without significant health and safety risk; (2) cooperative group trials; (3) industry trials, and (4) institutional transplant Pilot studies using standard (non-investigational) preparatory regimens and infusion products is not required by the PRMS Office and are reported ONLY to the IRB, as per instructions. For studies where AE event reporting to the PRMS Office is required, the PRMS Office confirms all agency notifications required by protocol have been submitted. The audit process (see Section V.C below) provides a mechanism for identifying AEs not reported to the PRMS Office.

B. Plan for Assuring that any Action Resulting in a Temporary or Permanent Suspension of an NCI-Funded Clinical Trial is Reported to the NCI Grant Program Director Responsible for the Grant.

Any actions leading to a recommendation to suspend an NCI-funded clinical trial are communicated formally to the Associate Director for Clinical Research. The Associate Director is ultimately responsible for assuring any action resulting in a temporary or permanent suspension of an NCI-funded clinical trial is reported to the NCI grant program director responsible for the grant.

C. Plan for Assuring Data Accuracy and Protocol Compliance

The Audit Committee (AC) audits investigator-initiated institutional protocols (except for non-therapeutic studies) and reports its findings to the DSMC, SRC, IRB and the Associate Director for Clinical Research. Cooperative Group trials are audited by the respective Groups, and industry-sponsored trials are audited by the company or its agent. Studies are eligible for audit the third month after the first accrual. All high-risk Pilot, Phase I, and Phase II trials will be reviewed by the Audit Committee semiannually. The audit committee will review low risk Pilot and Phase II trials and all Phase III trials no less than annually. At each audit, the records of at least one (1) randomly selected eligible subject, but otherwise no more than 10% of the total eligible subjects accrued, is audited.

For Phase I studies, the PRMS Administrator will notify the PI of the scheduled audits at the time of the accrual of the first subject to the study. For all other studies, the PRMS Administrator will notify the PI of an upcoming protocol audit and subjects selected no less than 60 days prior to the scheduled audit date.

The PRMS Administrator and/or the PRMS Auditor perform audits. Subject records selected for audit are chosen randomly from all eligible subjects enrolled. Subjects are audited once. Each chart is reviewed and evaluated for the following criteria:

1. Compliance with informed consent and eligibility requirements;
2. Treatment administration according to protocol guidelines;
3. Toxicity and adverse event reporting;
4. Appropriate follow-up.

Hospital records, as well as the protocol folder provided by the individual study coordinator or PI for each subject, are reviewed. Following each protocol audit, a report is prepared and submitted to the Audit Committee for review. The contents of the report include:

1. General observations regarding the audit process as a whole, and are not subject specific. Such observations might include a statement of general compliance with study criteria or the ease or difficulty the auditor experienced in completing a specific component of the audit.
2. Each individual case is reviewed according to the above criteria, and any unusual findings are described in detail.

These reports are circulated to the members of the AC. At each monthly AC meeting, the audits performed during the previous month are reviewed. At the conclusion of the meeting, the AC Chair communicates the results of the audit and the Committee's discussions in writing to the PI, the DSMC, the SRC and the Associate Director for Clinical Research. This letter and the audit report are filed with the protocol records in the PRMS Office. The Audit Committee may request further

information and/or follow-up from the PI. A response from the PI is expected within 30 days, although a more timely response may be required in some circumstances.

Should the audit reveal failure to comply with the approved study guidelines regarding adverse event reporting, eligibility criteria, stopping rules, accrual goals, quality data collection, etc. endangering the scientific integrity of the trial, the AC will report the audit results to the SRC and ask the SRC to determine whether:

1. Study accrual should be suspended, pending receipt of an acceptable plan for remedial action from the PI, or;
2. The study must be closed, or;
3. The study may continue.

TABLE 1

Adverse Event Reporting Requirements for Trials Supported by Grant or Contract Where NCI Holds IND

Unexpected Event		Expected Event	
Grades 2-3 Attributions of Possible, Probable, or Definite	Grades 4 and 5 Regardless of Attribution	Grades 1-3	Grades 4 and 5 Regardless of Attribution
Grade 2: Expedited report within 10 working days to IDB* Grade 3: Report by phone by IDB* within 24 hours. Expedited report to follow within 10 working days.	Report by phone to IDB within 24 hours. Expedited report to follow within 10 working days. Includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution. Any late death attributed to the agent (possible, probable, or definite) must be reported within 10 working days.	Expedited reporting NOT required.	Report by phone to IDB within 24 hours. Expedited report to follow within 10 working days. Includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution. Any late death attributed to the agent (possible, probable, or definite) must be reported within 10 working days.

*IDB = Investigational Drug Branch
Grade 1 reporting for Unexpected Event is not required.

FOR HOSPITALIZATION ONLY–Any medical event equivalent to the CTC Grade 3, 4 and 5, which precipitated hospitalization (or prolongation of existing hospitalization), must be reported regardless of expectation or attribution.

Expedited reporting may not be appropriate for specified expected adverse events. In those situations, AEs not requiring expedited reporting must be specified in the text of the approved protocol. For example, expected Grade 4 myelosuppression may not require expedited reporting.

TABLE 2-A

Adverse Event Reporting Requirements for Cooperative Group Trials Where NCI Holds IND

PHASE I STUDIES

Unexpected Event		Expected Event	
Grades 2-3 Attributions of Possible, Probable, or Definite	Grades 4 and 5 Regardless of Attribution	Grades 1-3	Grades 4 and 5 Regardless of Attribution
Grade 2: Expedited report within 10 working days to IDB*/CG+ Grade 3: Report by phone by IDB*/CG+ within 24 hours. Expedited report to follow within 10 working days.	Report by phone to IDB*/CG+ within 24 hours. Expedited report to follow within 10 working days. Includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution. Any late death attributed to the agent (possible, probable, or definite) must within 10 working days.	Expedited reporting NOT required.	Report by phone to IDB*/CG+ within 24 hours. Expedited report to follow within 10 working days. Includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution. Any late death attributed to the agent (possible, probable, or definite) must within 10 working days.

*IDB = Investigational Drug Branch, CG+ = Cooperative Group

FOR HOSPITALIZATION ONLY–Any medical event equivalent to the CTC Grade 3, 4 and 5, which precipitated hospitalization (or prolongation of existing hospitalization), must be reported regardless of expectation or attribution.

Expedited reporting may not be appropriate for specified expected adverse events. In those situations the AEs not requiring expedited reporting must be specified in the text of the approved protocol. For example, expected Grade 4 myelosuppression may not require expedited reporting.

TABLE 2-B

Adverse Event Reporting Requirements for Cooperative Group Trials Where NCI Holds IND

PHASE 2 AND PHASE 3 STUDIES

Unexpected Event		Expected Event	
Grades 2-3 Attributions of Possible, Probable, or Definite	Grades 4 and 5 Regardless of Attribution	Grades 1-3	Grades 4 and 5 Regardless of Attribution
Expedited report within 10 working days to IDB*/CG+	Report by phone to IDB*/CG+ within 24 hours. Expedited report to follow within 10 working days. Includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution. Any late death attributed to the agent (possible, probable, or definite) must within 10 working days.	Expedited reporting NOT required.	Report by phone to IDB*/CG+ within 24 hours. Expedited report to follow within 10 working days. Includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution. Any late death attributed to the agent (possible, probable, or definite) must within 10 working days.

*IDB = Investigational Drug Branch, CG+ = Cooperative Group

FOR HOSPITALIZATION ONLY–Any medical event equivalent to the CTC Grade 3, 4 and 5, which precipitated hospitalization (or prolongation of existing hospitalization), must be reported regardless of expectation or attribution.

Expedited reporting may not be appropriate for specified expected adverse events. In those situations the adverse events not requiring expedited reporting must be specified in the text of the approved protocol. For example, expected Grade 4 myelosuppression may not require expedited reporting.

TABLE

Adverse Event Reporting Requirements for Industry Trials Where a Corporate Sponsor Holds IND

Unexpected Event		Expected Event	
Grades 2-3 Attributions of Possible, Probable, or Definite	Grades 4 and 5 Regardless of Attribution	Grades 1-3	Grades 4 and 5 Regardless of Attribution
Grade 2: Expedited report within 10 working days to CS* Grade 3: Report by phone by CS* within 24 hours. Expedited report to follow within 10 working days.	Report by phone to CS* within 24 hours. Expedited report to follow within 10 working days. Includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution. Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.	Expedited reporting NOT required.	Report by phone to CS* within 24 hours. Expedited report to follow within 10 working days. Includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution. Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.

*CS = Corporate Sponsor

FOR HOSPITALIZATION ONLY–Any medical event equivalent to the CTC Grade 3, 4 and 5, which precipitated hospitalization (or prolongation of existing hospitalization), must be reported regardless of expectation or attribution.

Expedited reporting may not be appropriate for specified expected adverse events. In those situations the adverse events not requiring expedited reporting must be specified in the text of the approved protocol. For example, expected Grade 4 myelosuppression may not require expedited reporting.

TABLE

Adverse Event Reporting Requirements for Trials Where the Investigator Holds IND

Unexpected Event		Expected Event	
Grades 2-3 Attributions of Possible, Probable, or Definite	Grades 4 and 5 Regardless of Attribution	Grades 1-3	Grades 4 and 5 Regardless of Attribution
Grade 2: Expedited report within 10 working days to FDA Grade 3: Report by phone to FDA within 24 hours. Expedited report to follow within 10 working days.	Report by phone to FDA within 24 hours. Expedited report to follow within 10 working days. Includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution. Any late death attributed to the agent (possible, probable, or definite) must within 10 working days.	Expedited reporting NOT required.	Report by phone to FDA within 24 hours. Expedited report to follow within 10 working days. Includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution. Any late death attributed to the agent (possible, probable, or definite) must within 10 working days.

FOR HOSPITALIZATION ONLY–Any medical event equivalent to the CTC Grade 3, 4 and 5, which precipitated hospitalization (or prolongation of existing hospitalization), must be reported regardless of expectation or attribution.

Expedited reporting may not be appropriate for specified expected adverse events. In those situations the adverse events not requiring expedited reporting must be specified in the text of the approved protocol. For example, expected Grade 4 myelosuppression may not require expedited reporting.

TABLE

Adverse Event Reporting Requirements for Trials Involving Commercial Agents with No IND

Unexpected Event		Expected Event	
Grades 2-3 Attributions of Possible, Probable or Definite	Grades 4 and 5 Regardless of Attribution	Grades 1-2	Grades 4 and 5 Regardless of Attribution
Grade 2: Expedited report within 10 working days to FDA Grade 3: Report by phone to FDA within 24 hours. Expedited report to follow within 10 working days.	Report by phone to FDA within 24 hours. Expedited report to follow within 10 working days. Includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution. Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.	Expedited reporting NOT required.	Report by phone to FDA within 24 hours. Expedited report to follow within 10 working days. Includes all deaths within 30 days of the last dose of treatment with an investigational agent regardless of attribution. Any late death attributed to the agent (possible, probable, or definite) should be reported within 10 working days.

NOTE: USE MED WATCH FORM

FOR HOSPITALIZATION ONLY–Any medical event equivalent to the CTC Grade 3, 4 and 5, which precipitated hospitalization (or prolongation of existing hospitalization), must be reported regardless of expectation or attribution.

Expedited reporting may not be appropriate for specified expected adverse events. In those situations the adverse events not requiring expedited reporting must be specified in the text of the approved protocol. For example, expected Grade 4 myelosuppression may not require expedited reporting.

APPENDIX

Scientific Review Committee Membership (as of June 1, 2022)

Member	Department (Expertise)	Academic Title
David Kelly, PhD, Chair	Eppley Institute Faculty	Assistant Professor
Sarah Holstein, MD, PhD	Int Medicine Hematology/Oncology	Associate Professor
Deron Anderson	IRB Administrator	Office of Regulatory Affairs
Michael Baine, MD, PhD	Radiation Oncology	Assistant Professor
J. Baranowska-Kortylewicz, PhD	Radiation Oncology (Radiation Chemistry)	Professor
Vijaya Bhatt, MD	Int Medicine Hematology/Oncology	Associate Professor
Adrian Black, PhD	Eppley Institute Faculty	Assistant Professor
R. Gregory Bociek, MD, MSc	Adult Hem/Onc (Epidemiology/Lymphoma)	Professor
Donald Coulter, MD (Ad Hoc)	Pediatric Hematology/Oncology	Professor
Kristin Dickinson, PhD	CON-Omaha Division	Assistant Professor
Dalia Elgamal, PhD	Eppley Institute Faculty	Assistant Professor
Kurt Fisher, MD	Pathology/Microbiology	Assistant Professor
Krishna Gundabolu, MBBS	Adult Hem/Onc (Leukemia, Myeloma)	Assistant Professor
Gleb Haynatzki, PhD	COPH Biostatistics	Professor
M. Anne Kessinger, MD	Emeritus	Professor Emeritus
Kelsey Klute, MD	Int Medicine Hematology/Oncology	Assistant Professor
James Landmark, MD	Pathology/Microbiology (Blood Banking)	Emeritus Associate Professor
Quan Ly, MD	Surgical Oncology (GI/Pancreatic Cancer)	Professor
James Padussis, MD	Surgical Oncology	Assistant Professor
Jane Rips	Community Member	N/A
Carol Russell	Community Member	N/A
Zafar Sayed, MD	Otol-Head and Neck Surgery	Assistant Professor
Lynette Smith, PhD	COPH Biostatistics	Assistant Professor
Gary Yee, PharmD	College of Pharmacy (Pharmacy Practice)	Professor
Fang Yu, PhD	COPH Biostatistics	Associate Professor

APPENDIX

Data and Safety Monitoring Committee Membership (as of June 1, 2022)

Member	Department (Expertise)	Academic Title
Lori Maness-Harris, MD, Chair	Adult Oncology/Hematology (Transplantation Leukemia, MDS)	Associate Professor
Nicole Shonka, MD, Vice Chair	Adult Oncology/Hematology (Neuro-oncology, Sarcoma)	Associate Professor
R. Gregory Bociek, MD, MSC	Adult Oncology/Hematology (Transplantation, Lymphoma)	Professor
Jessica Maxwell, MD, MSc	Surgical Oncology	Assistant Professor
Avyakta Kallam, MBBS	Adult Oncology/Hematology (Lymphoma)	Assistant Professor
Alex Nester, MD	Adult Oncology/Hematology (Benign Hematology, Sickle Cell Disease, Bleeding Disorders)	Assistant Professor
Pavan Tandra, MBBS	Oncology/Hematology (Breast)	Assistant Professor
Chi (Kevin) Zhang, MD, PhD	Radiation Oncology (Brain and CNS)	Associate Professor
Daisy Dai, PhD	COPH Biostatistics, COPH, Associate Dean for Research	Professor
Jane Rips	Community Representative	

APPENDIX

Audit Committee Membership (as of June 1, 2022)

Member	Department (Expertise)	Academic Title
Elizabeth Reed, MD, Chair	Adult Oncology/Hematology (Breast Cancer)	Professor
M. Anne Kessinger, MD,	Adult Oncology/Hematology (Lung Cancer, Melanoma, Sarcoma)	Professor
Bhavina Sharma, MD	Adult Oncology/Hematology (Lung Cancer, Melanoma)	Assistant Professor
Jairam Krishnamurthy, MD	Adult Oncology/Hematology (Breast Cancer)	Assistant Professor
Alissa Marr, MD	Adult Oncology/Hematology (Lung Cancer, Melanoma)	Assistant Professor

APPENDIX

DSMC POLICIES AND PROCEDURES FOR STUDIES BEING CONDUCTED AT MORE THAN ONE SITE WITH UNMC AS THE STUDY SOURCE (i.e. Sponsor)

I. PURPOSE:

The Fred & Pamela Buffett Cancer Center Data and Safety Monitoring Committee (DSMC) is assigned the responsibility of monitoring the safety of all research participants in clinical research studies sponsored by the Fred & Pamela Buffett Cancer Center (FPBCC) members, as outlined in the UNMC Eppley Cancer Center revised Institutional Data and Safety Monitoring Plan, Version 4, dated September 8, 2020.

In addition to the policies outlined in the Cancer Center's DSMC Policies and Procedures**, the following policies apply to all cancer-related Investigator-initiated Institutional and Multi- institutional treatment studies sponsored by UNMC and/or its Associated Locations and conducted by at least one additional participating site.**

II. DEFINITIONS:

A. UNMC ASSOCIATED LOCATIONS

UNMC/NMC Associated Locations include, but are not limited to, the Bellevue Medical Center, Village Pointe Medical Center, NE Orthopedic Hospital, and UNMC/NMC Clinics. Children's Hospital and Medical Center is NOT included.

B. PARTICIPATING SITE/S

The previous definitions of "Affiliate" and "Participating" sites are no longer valid. All sites other than UNMC/NMC and Associated Locations are now considered "Participating" sites. This includes Children's Hospital and Medical Center.

III. CLINICAL RESEARCH STUDIES REQUIRING DSMC REVIEW:

All cancer-related Investigator-initiated Institutional and Multi-institutional treatment studies sponsored by UNMC and/or its Associated Locations fall under the purview of the DSMC. These clinical research study/ies must be monitored by the DSMC or a board specifically designed for the individual study. The level of monitoring is determined by the type of study and potential risks.

IV. DSMC RESPONSIBILITIES:

A. Responsibilities of the UNMC Principal Investigator (PI) andCoordinator:

1. Conducts continuous review of data and subject safety.
2. Ensures all AEs and SAEs are reported to the Cancer Center's Protocol Review and Monitoring System (PRMS) Office and to the UNMC IRB as specified in Section 9.0 of the currently approved study document (or the equivalent adverse event reporting).
3. Distributes the DSMP to the Participating Site/s and ensures adherence to the Adverse Event Reporting Guidelines by all participating institutions.
4. Conducts an initial site visit prior to opening a study to accrual at a ParticipatingSite.
5. Provides ongoing guidance and direction, as needed, to the Participating Site Investigator/Consenting MD and Coordinator regarding study specific data and subject safety.
6. Submits study, data collection and adverse event report forms to the FPBCC Audit Committee (AC), Data and Safety Monitoring Committee (DSMC), and Scientific Review Committee (SRC) for approval.
7. Provides the approved study, data collection, and adverse event report forms to the

Participating Site.

8. Ensures all study specified adverse events from Investigator-initiated Institutional Pilot, Phase I, Phase II, and Phase III studies are reported on standard adverse event reporting forms directly to the PRMS Office and separately to the IRB.

B. Responsibilities of the Participating Site Investigator/Consenting MD and Coordinator:

1. Conducts continuous review of data and subject safety at the ParticipatingSite.
2. Ensures all adverse events are reported to the UNMC PI as specified in Section 9.0 of the currently approved study document (or the equivalent adverse event reporting section.
3. Acts as liaison between the DSMC and the Participating Site Investigator and/or Consenting MD as needed.
4. Following the completion of the DSMC review, ensures appropriate follow-up and/or changes are completed as requested by the DSMC.

C. Responsibilities of the Cancer Center PRMS Office:

1. Provides ordination/training to the Participating Site Coordinator prior to opening a study to accrual at Participating Site regarding Audit, DSMC, or SRC policies and procedures. Provides ongoing guidance and direction, as needed, to the Participating Site Coordinator.
2. Communicates in writing the study's adverse event summary and the results of the DSMC review of the study to the SRC and the Associate Director of Clinical Research.
3. Forwards the DSMC's recommendations regarding changes to the study or study conduct to the Associate Director of Clinical Research for action.
4. Sends notification of the impending DSMC review to the UNMC PI and Study Coordinator at least 30 days prior to the scheduled DSMC review date.

V. DSMC MONITORING OF MULTI-INSTITUTIONAL STUDIES WHERE UNMC IS THE LEAD SITE (i.e. Study Source or Sponsor):

A. Clinical research studies for all Multi-institutional studies with one or more participating sites and with UNMC as the lead site and study source (i.e. sponsor) must clearly outline the reporting requirements and procedures for all participating site/s.

B. Study sections pertaining to these reporting requirements and procedures must be approved by the DSMC prior to SRC review and approval.

C. The following issues must be addressed within the study for Multi-institutional studies with participating sites:

1. The study may state the DSM Committee or Board at a participating site will monitor all AEs and SAEs on-site. However, this designation, along with the reporting procedures at the participating site/s, must be approved by the DSMC.
2. If the DSMC/B at a participating site/s is approved as the monitoring board for AEs and SAEs, the participating site/s must agree in writing to: 1) forward their AE DSM reports to the DSMC at regularly planned intervals consistent with the DSMC review schedule; and 2) to fully report all SAEs to the DSMC.
3. The UNMC PI and/or their designee will be responsible for: 1) incorporating the AE/SAE data received from participating site/s into one DSMC Worksheet for all participating sites; 2) submitting the combined worksheet to the DSMC at regularly scheduled intervals; and 3) ensuring all SAEs for all participating sites are fully reported and submitted to the DSMC.

VI. INSTITUTIONAL REVIEW BOARD:

If a participating site does not have their own Institutional Review Board (IRB), the UNMC IRB will be the IRB of record for clinical research study/ies sponsored by UNMC and conducted by at least one additional participating site.

VII. DSMC DOCUMENTATION:

All DSMC documentation will be maintained in the Cancer Center PRMS Office (i.e. minutes, letters). In addition, copies of all DSMC related documents will be maintained at the Participating

Site.

VIII. INTRANET AND OPEN FORUM COMMUNICATIONS:

Current DSMC Policies and Procedures may be accessed on the intranet at http://www.unmc.edu/cancercenter/clinical/prms.html. Periodic open forums are scheduled with study coordinators and PIs to communicate and clarify DSMC policies and procedures and obtain feedback to streamline and facilitate the DSMC review process.

Please note: With the large number of IITs currently under the purview of the PRMS office, efficiencies in our internal processes must be created to optimize our workflows. Moving forward, all questions which arise outside of the open forums regarding Audit and DSMC must be submitted via email OR a meeting must be scheduled. Please send a meeting invite (including conference room number) to the Clinical Trials Regulatory Specialist to discuss any questions you may have regarding Investigator-Initiated Protocols.

Please note: the Clinical Trials Regulatory Specialist will only answer questions regarding PRMS Committee policy and/or reporting requirements as defined in the approved protocol and reserves the right to redirect questions to be asked of the IIT Office, Study Staff or Investigator.

Questions requiring immediate assistance must be submitted via email with a **high** priority status.

UNMC FRED & PAMELA BUFFETT CANCER CENTER

Data and Safety Monitoring Committee
Report for Phase 1 Studies

IRB# Choose an item. **PI:** Choose an item.

TITLE: Choose an item.

Report date: Click or tap to enter a date.

Date last review Submitted: Click or tap to enter a date. **Date of last DSMC Review:** Click or tap to enter a date.

SECTION I: PROTOCOL STAFF

Study Coordinator: Choose an item.

Study Nurse: Choose an item.

Personnel responsible for report: Choose an item.

SECTION II: PROTOCOL STATUS

☐ Open to Accrual

☐ On Hold

On Hold Date: Click or tap to enter a date. Hold Reason: Click or tap here to enter text.

☐ Study Closed to Accrual (CTA) – subjects on study-related therapy

CTA date: Click or tap to enter a date. CTA Reason: Click or tap here to enter text.

☐ Study CTA – all subjects off study-related treatment (*Final Scheduled Report*)
Date last subject received study-related treatment: Click or tap to enter a date.

SECTION III: SINGLE OR MULTI-SITE STUDY

☐ Single Site Study (If single site study – do no complete the rest of Section III)

☐ Multi-Site Study (If Multi-Site Study, list all participating sites)

Sites: Click or tap here to enter text.

SECTION IV: ACCRUAL – SINCE LAST SCHEDULED REVIEW and OVERALL

A. Newly enrolled patients since last scheduled DSMC review:

a. Number of new subjects registered at UNMC since last scheduled DSMC review:
Click or tap here to enter text.

b. Number of new subjects enrolled at each participation site since last scheduled DSMC review (*only for Multi-Site studies*): Click or tap here to enter text.
c. Number of new subject enrolled at all sites including UNMC since last scheduled DSMC review (only for Multi-Site studies): Click or tap here to enter text.

B. Total number of subjects enrolled since study activation:

a. Total number of subjects enrolled on study at UNMC since activation: Click or tap here to enter text.
b. Total number of patients enrolled at each participating site since activation (*only for Multi-site studies*): Click or tap here to enter text.
c. Total number of patients enrolled at all sites including UNMC since activation (*only for Multi-site studies*): Click or tap here to enter text.

SECTION V: TOTAL ENROLLED, WITHDRAWN and INELIGIBLE SINCE ACTIVATION

Provide the following information: (If this is Single-Site study, *do not complete the Multi-Site section*)

Site	Total # enrolled at UNMC	Total # withdrawn without receiving treatment at UNMC	Total # ineligible at UNMC

SECTION VI: FOR *MULTI-PHASE* STUDIES ONLY – TOTAL ENROLLED, WITHDRAWN and INELIGIBLE

Current enrollment to each phase of this protocol:

Phase	Date last subject was enrolled to this phase	Total # of subjects enrolled to this phase	Total # of subjects enrolled to this phase	Total # of subjects enrolled to this phase at all sites

SECTION VII: INTERIM ANALYSIS (IA) and STOPPING RULES

A. Does the protocol include an interim analysis?

☐ Yes ☐ No *If yes, answer items 1 and 2 below..*

1. Provide IA as defined in the protocol: Click or tap here to enter text.
2. Provide the time-frame for completing the IA: Click or tap here to enter text.

B. Does the protocol contain a stopping rule for safety?

☐ Yes ☐ No *If yes, answer item 1 below.*

1. Provide details as outline in the protocol: Click or tap here to enter text.

C. Does the protocol contain a stopping rule for efficacy?

☐ Yes ☐ No *If yes, answer item 1 below.*

1. Provide details as outlined in the protocol: Click or tap here to enter text.

SECTION VII: DOSE LEVEL(S) STUDIED AT EACH PARTICIPATING SITE

Provide the following information separately for each dose level studied at each participating site:

Dose level(s) studied at UNMC:

Dose Level	*Dose & Schedule of Agents*	*Total # of subjects enrolled dose/schedule*	*Total # of subjects withdrawn without receiving treatment*	*Total # ineligible*

For Multi-Site Studies ONLY: (duplicate the table for each participating site)

Participating Site: Click or tap here to enter text.

Dose Level	*Dose & Schedule of Agents*	*Total # of subjects enrolled dose/schedule*	*Total # of subjects withdrawn without receiving treatment*	*Total # ineligible*

2nd Participating Site: Click or tap here to enter text.

Dose Level	*Dose & Schedule of Agents*	*Total # of subjects enrolled dose/schedule*	*Total # of subjects withdrawn without receiving treatment*	*Total # ineligible*

SECTION VII: ADVERSE EVENT REPORTING WORKSHEET

Complete and attach an Adverse Event Reporting Worksheet (template located on the PRMS website), listing all reportable adverse events. If this study is a Multi-Site protocol, include all reportable adverse events from *all sites*.

Worksheet must include:

1. The subjects Study ID (including site ID) and initials (if necessary). **DO NOT USE MRNs**
2. The Site where the subject enrolled.
3. The **CTCAE term** required to define the event.
4. New events, not found on previous report: Place an asterisk (*) before the CTCAE term to mark new events.
5. The state Date of the AE/SAE.
6. The end Date of the AE/SAE.
7. The Attribution of the AE/SAE.

Please note: If an update has been made to a previously reviewed event, place a strike through (~~abc~~) on the event and type the update on the same line as the previous event. In the comment section, state why a change was made.

_____ Click or tap to enter a date.

Signature of person completing report Date

_____ Click or tap to enter a date.

Signature of Principal Investigator Date

UNMC FRED & PAMELA BUFFETT CANCER CENTER

Data and Safety Monitoring Committee
Report for Pilot, Phase 2 and Phase 3 Studies

IRB# Choose an item. **PI:** Choose an item.

TITLE: Choose an item.

Report date: Click or tap to enter a date. **Date of last DSMC Review:** Click or tap to enter a date.

SECTION I: PROTOCOL STAFF

Study Coordinator: Choose an item.

Study Nurse: Choose an item.

Personnel responsible for report: Choose an item.

SECTION II: PROTOCOL STATUS

☐ Open to Accrual

☐ On Hold

On Hold Date: Click or tap to enter a date. Hold Reason: Click or tap here to enter text.

☐ Study Closed to Accrual (CTA) – subjects on study-related therapy

CTA date: Click or tap to enter a date. CTA Reason: Click or tap here to enter text.

☐ Study CTA – all subjects off study-related treatment (*Final Scheduled Report*)
Date last subject received study-related treatment: Click or tap to enter a date.

SECTION III: SINGLE OR MULTI-SITE STUDY

☐ Single Site Study (If single site study – do no complete the rest of Section III)

☐ Multi-Site Study (If Multi-Site Study, list all participating sites)

Sites: Click or tap here to enter text.

SECTION IV: ACCRUAL – SINCE LAST SCHEDULED REVIEW and OVERALL

A. Newly enrolled patients since last scheduled DSMC review:

a. Number of new subjects registered at UNMC since last scheduled DSMC review:
Click or tap here to enter text.

b. Number of new subjects enrolled at each participation site since last scheduled DSMC review:

Click or tap here to enter text.

c. Number of new subject enrolled at all sites including UNMC since last scheduled DSMC review:

Click or tap here to enter text.

B. Total number of subjects enrolled since study activation:

a. Total number of subjects enrolled on study at UNMC since activation: Click or tap here to enter text.

b. Total number of patients enrolled at each participating site since activation: Click or tap here to enter text.

c. Total number of patients enrolled at all sites including UNMC since activation: Click or tap here to enter text.

SECTION V: TOTAL ENROLLED, WITHDRAWN and INELIGIBLE SINCE ACTIVATION

Provide the following information:

Site	Total enrolled & received treatment	Total withdrawn without receiving treatment	Total found to be a screen failure

SECTION VI: INTERIM ANALYSIS (IA) and STOPPING RULES

A. Does the protocol include an interim analysis? *If yes, answer items 1 and 2 below*

☐ Yes ☐ No

1. Provide IA as defined in the protocol: Click or tap here to enter text.
2. Provide the time-frame for completing the IA: Click or tap here to enter text.

B. Does the protocol contain a stopping rule for safety?

☐ Yes ☐ No *If yes, answer item 1 below.*

1. Provide details as outline in the protocol: Click or tap here to enter text.

C. Does the protocol contain a stopping rule for efficacy?

☐ Yes ☐ No *If yes, answer item 1 below.*

1. Provide details as outlined in the protocol: Click or tap here to enter text.

SECTION VII: ADVERSE EVENT REPORTING WORKSHEET

Complete and attach an Adverse Event Reporting Worksheet (template located on the PRMS website), listing all reportable adverse events. If this study is a Multi-Site protocol, include all reportable adverse events from *all sites*.

Worksheet must include:

1. The subjects Study ID (including site ID) and initials (if necessary). **DO NOT USE MRNs**
2. The Site where the subject enrolled.
3. The **CTCAE term** required to define the event.
4. New events, not found on previous report: Place an asterisk (*) before the CTCAE term to mark new events.
5. The state Date of the AE/SAE.
6. The end Date of the AE/SAE.
7. The Attribution of the AE/SAE.

Please note: If an update has been made to a previously reviewed event, place a strike through (~~abc~~) on the event and type the update on the same line as the previous event. In the comment section, state why a change was made.

Click or tap here to enter text.
Printed name of person completing report

Click or tap to enter a date.
Date

_____
Signature of Principal Investigator

_____
Date

UNMC FRED & PAMELA BUFFETT CANCER CENTER

Data and Safety Monitoring Committee
Dose Level Change Report – For Phase 1 Protocols

IRB# Choose an item.
TITLE: Choose an item.
Report date: Click or tap to enter a date.

PI: Choose an item.

Date of last DSMC Review: Click or tap to enter a date.

SECTION I: PROTOCOL STAFF

Study Coordinator: Choose an item.
Study Nurse: Choose an item.
Personnel responsible for report: Choose an item.

SECTION II: PROTOCOL STATUS

☐ Open to Accrual
☐ On Hold
On Hold Date: Click or tap to enter a date. Hold Reason: Click or tap here to enter text.
☐ Study Closed to Accrual (CTA) – subjects on study-related therapy
CTA date: Click or tap to enter a date. CTA Reason: Click or tap here to enter text.
☐ Study CTA – all subjects off study-related treatment (*Final Scheduled Report*)
Date last subject received study-related treatment: Click or tap to enter a date.

SECTION III: INSTRUCTIONS

a. Previous dose level being studied: Click or tap here to enter text.
b. Current dose level being studied: Click or tap here to enter text.
c. Date of change from previous dose to current dose: Click or tap to enter a date.
d. Reason for change: Click or tap here to enter text.
e. Provide the following information separately for each dose level studied:

Note: For studies sponsored by UNMC (*whether being conducted only at UNMC or at one or more additional participating institutions*) include information on **all subjects registered at all participating sites**.

Dose Level	Agent Name, Dose & Schedule	# Enrolled per Dose Level	Date of Dose Level Change	Reason for Dose Level Change (i.e. per protocol, MTD, DLT)

_____ _____

Signature of person completing report Date

_____ _____

Signature of Principal Investigator Date

Adverse Event Reporting Worksheet for Protocol							IRB#	
PI:		Study Coordinator/Contact:					Date Report Completed:	
Site [1]	Patient Identifier[2]	Adverse Event [3]	Start Date	End date	Grade [4]	Attribution [5]	Serious [6]	Notes

[1] Enter the site where the subject was enrolled. A unique site identifier may be used as long as a legend for these identifiers is included on the worksheet

[2] **Only use Study IDs for Patient Identifier. Initials may be added if necessary. DO NOT use Subject MRNs.**

[3] Mark all new events since the last report with an * in front of the adverse event

[4] Use CTCAE version determined by the protocol.

[5] Code as: unrelated or unlikely, possibly, probably or definitely related

[6] Enter "Yes" for all serious adverse events or "No" for non-serious events

Note: The DSMC requires reporting of all toxicities grade 3 or higher (current CTCAE criterion), expected or unexpected, and regardless of attribution unless stated otherwise in the protocol.

Site [1]	Patient Identifier[2]	Adverse Event [3]	Start Date	End date	Grade [4]	Attribution [5]	Serious [6]	Notes
PI Signature & Date: _____								