

## Study-Specific DSM Plan for Investigator-Initiated Trials

**Section A. Guidance for developing a study-specific DSMP using this form.**

**UVM Cancer Center** **Data & Safety Monitoring Plan (DSMP)** **For Investigator-Initiated Cancer Trials**

Investigators must develop a study-specific DSMP on the following form for all Investigator-Initiated Trials (IITs), including both clinical trials and observational studies (defined below). The DSMP must be included in the original submission of the protocol as a supplemental document to the Protocol Review and Monitoring Committee (PRMC). The PRMC will review the DSMP as part of the initial review of the study. Following PRMC assignment of the study risk level and approval of the DSMP, the UVMCC Data Safety and Monitoring Committee (DSMC) will be informed by the PRMC, which will subsequently guide the frequency of DSMC review of the study (quarterly, semi-annually, annually, or not at all), based on the risk level.

The DSMP should reflect the level of risk associated with the study. The purpose of the DSMP is to assure the safety of human subjects, the validity of data, and appropriate termination steps. The essential elements of the plan include:

**1. What data is to be monitored**

**2. Who is responsible for monitoring and how often**

**3. Reporting plan for communicating findings to IRB/Sponsor/Federal Agencies**

**4. Reporting plan for adverse events**

**5. Endpoints Proposed**

**6. Plans for assuring data accuracy and protocol compliance**

If an IIT involves a blinded study design, then a description of the planned randomization process (not the actual randomization schema) and the specific criteria and procedures for unblinding of treatment assignment, if required, should be included in the study-specific DSMP.

Additionally, special measures of how outcome data will be handled during data and safety review activities of the assigned DSMB/DSMC must be specified within the study-specific DSMP. For studies that remain blinded, outcome data should not be made available to individuals outside of the DSMC.

*If you have questions about preparing the DSMP, contact the DSMC and PRMC Coordinator at 802-656-2967.*

**Definitions:**

*Investigator-initiated trial (IIT):* A research study written and overseen by a local physician or professional. This research study could be an interventional trial or an observational study.

*Clinical trial:* A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

*Interventional trial:* A study in which a treatment, procedure, or other action is directed by the protocol and taken to prevent or treat disease, or improve health in other ways (e.g. drug therapies, medical devices, behavior changes like exercise or diet, educational programs, etc.).

*Observational study:* A study in which individuals are observed or certain outcomes are measured but no attempt is made to affect the outcome (no treatment or procedure is required by the protocol). Examples could include collection of questionnaire data only and non-invasive biospecimen collection (e.g. blood, saliva).

**Section B. PRMC-Required Form for a Study-Specific DSM Plan**

**Is this study considered an Interventional trial as defined in Section A?**  [ ]  Yes [ ]  No

If yes, please complete the entire form in Section B.

If no, skip Sections 1-2 and complete the Sections 3-5.

**Data & Safety Monitoring Plan for**

*[Insert title]*

*[Insert Study ID/CTO #]*

*[Insert Principal Investigator]*

*Created: [Insert Date this form is Completed]*

**1. Trial Safety: Identification of risks and plans to minimize risk**

***NOTE:*** *skip Section 1 if your protocol is an observational study.*

1.1. What risks are **expected** due to the intervention in this protocol?

**Expected:** A risk identified in nature, severity or frequency in the study documentation (protocol, consent, Investigator Brochure, package insert etc.) is considered an expected risk.

* The risks should be consistent with those in the consent form and the investigator’s brochure (if applicable), although they should be written in technical terms in the protocol and in lay terminology in the consent form.
* List the most serious risk first.
* If this is already in the protocol document, you may reference the protocol’s risk section.

|  |  |
| --- | --- |
| **Expected Risks related to [Insert Intervention]** | **Frequency** |
|  | [ ] Occurs frequently,[ ] Occurs infrequently[ ] Occurs rarely[ ] Frequency unknown |
|  | [ ] Occurs frequently,[ ] Occurs infrequently[ ] Occurs rarely[ ] Frequency unknown |
| **Expected Risks related to [Insert Intervention]** | **Frequency** |
|  | [ ] Occurs frequently,[ ] Occurs infrequently[ ] Occurs rarely[ ] Frequency unknown |
|  | [ ] Occurs frequently,[ ] Occurs infrequently[ ] Occurs rarely[ ] Frequency unknown |

*(NOTE: Add expected risks sections as necessary.)*

1.2. List by bullet format a summary of planned safety tests/procedures/observations to be performed as measures to protect participants against foreseeable risks.

1.3. Check the criteria below under which an INDIVIDUAL SUBJECT’S study treatment or study participation would be *stopped* or *modified*.

[ ]  At subject, PI, or study team member request

[ ]  If the subject had a Serious Adverse Event (SAE) deemed related to study

[ ]  Other: *specify*

[ ]  Please provide the language and the section number directly from the protocol:

1.4. Check the criteria under which THE ENTIRE STUDY would need to be stopped. These are called stopping rules for early termination of the entire study. (*Regardless of whether the study is sponsored or not, be sure to include any criteria for which the local PI would halt the study at UVMMC/UVMCC.)* (*Check all that apply*)

[ ]  Based on a formal safety review or futility test, as described in the protocol.

[ ]  Other: *specify*

[ ]  Please provide the language and the section number directly from the protocol:

1.5. Describe the criteria for breaking the blind/mask:

[ ]  *Specify:*

[ ]  Not Applicable (N/A) – Not blinded/masked

[ ]  Please provide the language and section number directly from the protocol:

1.6. How will subject withdrawals/dropouts be reported to the IRB prior to study completion? (*Check all that apply*)

[ ]  IRB annual continuing renewal submission

 [ ]  Other type of list/form *(please attach)*

1.7. Incidental Findings: Describe the plan for management of incidental findings and give examples of possible incidental findings (e.g., potential structural abnormality discovered during a scan):

###### 2. Adverse Events

***NOTE:*** *skip Section 2 if your protocol is an observational study.*

2.1. How will you define **adverse events (AE)** for this study? (*Check if you concur, or fill-in other*)

[ ]  An adverse event (AE) will be considered any undesirable sign, symptom or medical or psychological condition **even if the event is** **not considered to be related** to the investi- gational drug/device/intervention. Medical conditions/diseases present before starting the investigational drug/intervention will be considered AEs only if they worsen after starting study treatment/intervention. An AE is also any undesirable and unintended effect of research occurring in human subjects as a result of the collection of identifiable private information under the research. AEs also include any problems associated with the use of an investigational device that adversely affects the rights, safety or welfare of subjects.

[ ]  Other: *(insert definition:* )

2.2. How will you define **serious adverse events (SAEs)**?

[ ]  A serious adverse event (SAE) will be considered any undesirable sign, symptom, or medical condition which is fatal, life-threatening, requires or prolongs inpatient hospitalization, results in persistent or significant disability/incapacity, constitutes a congenital anomaly/ birth defect, is medically significant and which the investigator regards as serious based on appropriate medical judgment. An important medical event is any AE that may not result in death, be life-threatening, or require hospitalization but may be considered an SAE when, based upon appropriate medical judgment, it may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in the definitions of SAEs.

[ ]  Any serious psychological and emotional distress resulting from study participation (suggesting need for professional counseling or intervention).

2.3. Will ALL AEs above be collected/ recorded?

**[ ]** Yes

[ ]  No- If no, describe criteria for which AEs will be collected/recorded

 *Specify:*

2.4. How will AE data be collected/ recorded? (*Check all that apply*)

[ ]  Paper AE forms/source documents (please attach a copy of this form if possible)

[ ]  Electronic Spreadsheet *(e.g electronic Excel sheets)*. Describe where information will be saved and who will be managing and entering data. *Specify:*

[ ]  Database (*specify name/type of database(s)*:       Describe where database will be saved and who will be managing and entering data. *Specify:*

2.5. How will AEs be classified/graded? (C*heck* ***all*** *that apply*)

[ ]  World Health Organization Criteria (WHO)

[ ]  NCI Common Toxicity Criteria for Adverse Events (CTCAE), Version 5.0

[ ]  Other: *(specify*)

2.6. What scale will the PI use when evaluating the relatedness of AEs to the study participation? (C*heck* ***all*** *that apply.*)

[ ]  The PI will determine the relationship of AEs to the study

 using the following scale:

Definite: AE is clearly related in time and a direct association can be demonstrated to the study intervention.

Probable: AE is reasonably related in time and is more likely explained by the study intervention than by other causes.

Possible: AE may be reasonably related in time and the AE can be explained equally well by causes other than the study intervention.

Unlikely: A potential relationship could exist with the study intervention, but the AE is most likely explained by other causes.

Unrelated: AE is clearly not related to intervention and can be fully explained by another cause. This other cause should be provided.

[ ]  The PI will use an alternative attribution scale. (*specify*)

2.7. When will recording/reporting of AEs begin?

[ ]  After subject signs consent

[ ]  After subject begins study drug/ device placement/intervention /study-related procedure/specimen collection

[ ]  Other: *(specify)*

2.8. When will the recording/reporting of AEs end?

[ ]  End of study drug/device/intervention/participation

[ ]  30 days post study drug/device/intervention

[ ]  Subject completes intervention and follow up period of protocol

[ ]  Other: *(specify)*

2.9. Please modify the following table to describe details of AE reporting. [**The language provided below is an example and should not be included in your DSM Plan if it does not follow the PI’s plan for monitoring AEs or other reportable events. Please modify if additional reporting to the FDA or other supporting sponsor is required.]**

|  |  |  |  |
| --- | --- | --- | --- |
| **Type of Event** | **To whom will it be reported** | **Time Frame for Reporting** | **How to report?** |
| Death of a research subject unless the death is expected (e.g. due to disease progression). | UVMCC DSMC and designated IRB, if applicable per IRB policy. | DSMC: Within 24 hours | DSMC: Email  |
| Serious Adverse Event (SAE), *regardless of relatedness of expectedness* | UVMCC DSMC and designated IRB, if applicable per IRB policy. | DSMC: Within 10 working days from the time the study team received knowledge of the event. | DSMC: Email  |
| [May insert additional expedited reporting requirements] |  |  |  |

**3. Unanticipated Problems and Protocol Deviations**

3.1. This is the definition of an **unanticipated problem**: (C*heck if you concur, or fill-in other*)

[ ]  An unanticipated problem is any event/experience that meets ALL 3 criteria below (*see UVM IRB Policy*):

* unexpected (in terms of nature, severity, or frequency) given: (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
* related or possibly related to a subject's participation in the research;
* suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.

[ ]  Other: *(insert definition:*      )

3.2. One definition of **a protocol deviation is below.** Please check the first box if that is the definition that will be used to describe deviations in this study. If not, please provide an alternative definition.

[ ]  A protocol deviation **is any variance from the protocol involving a subject or subjects that is not approved by the IRB prior to its initiation or implementation, and occurs when a member of the study team departs from the IRB-approved protocol in any way without the investigator first obtaining IRB approval (*See UVM IRB Policy*).**

[ ]  Other: *(insert definition:*      )

3.3. When will recording/reporting of Unanticipated Problems and Protocol Deviations begin?

[ ]  After subject signs consent

[ ]  After subject begins study drug/ device placement/intervention /study-related procedure/specimen collection

[ ]  Other: *(specify)*

3.4. When will the recording/reporting of Unanticipated Problems and Protocol Deviations end?

[ ]  End of study drug/device/intervention/participation

[ ]  30 days post study drug/device/intervention

[ ]  Subject completes intervention and follow up period of protocol

[ ]  Other: *(specify)*

3.5. Please modify the following table to describe details of Unanticipated Problem, and Protocol Deviation reporting. [**The language provided below is an example and should not be included in your DSM Plan if it does not follow the PI’s plan for reportable events. Please modify if additional reporting to the FDA or other supporting sponsor is required.]**

|  |  |  |  |
| --- | --- | --- | --- |
| **Type of Event** | **To whom will it be reported** | **Time Frame for Reporting** | **How to report?** |
| Unanticipated Problems that are not AEs or protocol deviations. | Designated IRB, if applicable per IRB policy. | As per IRB policy. | As per IRB policy. |
| [May insert additional expedited reporting requirements] |  |  |  |

**4.** **Data Collection Methods and Other Study Operations**

4.1. Describe the endpoints of the study.

[ ]  Please see protocol Section:

[ ]  Other: *specify*

4.2. How will the endpoint data be collected/recorded? **(***Check all that apply***)**

[ ]  Protocol-specific Case Report Forms (CRFs) (**attach CRFs if in-house**)

[ ]  Source documents

[ ]  Database: *specify*

[ ]  Other:

4.3. Describe where the CRFs or database will be stored and accessed at the time of future audits.

*Specify*

4.4. If this is a multicenter trial (*for example, this includes studies opened at collaborating site Dartmouth Hitchcock Medical Center and affiliate sites Central Vermont Medical Center and Glens Falls Hospital*) describe how patient will be registered and unique patient IDs assigned.

*Specify*

*[ ]  NA – Not multi-center*

4.5. If this is a randomized study, describe how the randomization will be completed. Who will maintain access of the randomization schema?

*Specify*

*[ ]  NA – Not randomized*

4.6. If this is a blinded study, describe how the blinding will occur. Who will maintain access of the blinded assignments?

*Specify*

*[ ]  NA – Not blinded/masked*

4.7. If this study involves additional correlative sub-studies, please describe how specimens will be linked to the other research data and overall documentation of chain of custody.

*Specify*

*[ ]  NA – There are no correlative studies*

4.8. Please review the **UVMCC DSM Report** and confirm that this data can be provided on a routine basis to the UVMCC DSMC.

[ ]  Yes

[ ]  Yes, but with the tables in a different format. (Please note that the DSMC may ask that you alter this format upon their review.)

**5. Data and Safety Oversight Responsibility**

5.1. Who is responsible for overseeing the study data (*i.e., Who is looking at data* in aggregate form to identify trends?) (Check all that apply)

[ ]  The UVMCC DSMC *(skip question 5.2. and go to question 5.3.)*

[ ]  Industry Sponsored-designated DSMB/DSMC/Medical Monitor

*[ ]* Non-Industry Sponsored (other academic center, NIH) designated DSMB/DSMC/Medical Monitor (*If your study is NIH funded, please check with the center to determine if they require a DSMB for this study)*

[ ]  Other: *specify*

5.2. What is the composition of the reviewing body and how is it affiliated with the sponsor? *Note: Members of the study team may NOT also be members of the DSMB.*

[ ]  List:

5.3. Answer this question ONLY if the PI is the ONLY person overseeing the safety data for this study. (*Note: in this case you will have checked the first box for question* #5.1. "*UVMCC Data Safety and Monitoring Committee.”)*

Please check aggregate reviews that will occur by the PI *(Check all that apply*):

[ ]  All AEs

[ ]  Unanticipated Problems

[ ]  Protocol violations

[ ]  Audit results

[ ]  Application of dose finding escalation/de-escalation rules

[ ]  Application of study designed stopping/decision rules

[ ]  Early withdrawals

[ ]  Whether the study accrual pattern warrants continuation/action

[ ]  Endpoint data

[ ]  Other: (*specify*)

5.4. Answer this question ONLY if the PI is the ONLY person responsible for overseeing the safety of the study. (*Note: in this case you will have checked the first box for question #5.1. "UVMCC Data Safety and Monitoring Committee.")*

How often will aggregate review occur by the PI?

[ ]  Annually

[ ]  Semi-annually

[ ]  Quarterly

[ ]  Monthly

[ ]  Other: *(specify )*

*Note that for IITs the PRMC will recommend to the DSMC to review the DSM Report either annually, semi-annually, or quarterly. This DSMC review is separate from the PI’s own review.*

5.5. Answer this question ONLY if this study has someone besides the PI overseeing the safety data. *(Note: in this case you will have checked a choice other than the first box for Question #5.1., for example* “*Industry Sponsored-designated DSMB/DSMC/Medical Monitor*.*”)*

How often will a report, regarding the outcome of the reviews, be sent to the PI from the oversight body listed in 5.1?

[ ]  Every six months

[ ]  Once a year

[ ]  Other: *(specify)*

**Thank you. Please submit this Study-Specific DSM Plan with your initial protocol submission to the UVM Cancer Center PRMC.**