

INSTRUCTIONS: This file contains templates for protocol language for DSMPs for Minimal Risk, Moderate Risk and High Risk. After choosing the appropriate template, it should be modified to reflect the unique attributes of the study.

Example: Minimal Risk DSMP

The principal investigator is responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews at the specified frequency [*e.g., monthly, quarterly, etc.*]. During the review process the principal investigator will evaluate whether the study should continue unchanged, require modification/amendment, continue or close to enrollment.

Either the principal investigator, the Human Investigation Committee (HIC) or [*enter the names of other oversight bodies that have this authority, e.g., QUACS*] have the authority to stop or suspend the study or require modifications.

This protocol presents minimal risks to the subjects and adverse events or other problems are not anticipated. In the unlikely event that such events occur, serious and unanticipated and related adverse events or unanticipated problems involving risks to subjects or others will be reported in writing within 48 hours to the HIC (using the appropriate HIC forms from the website) and any appropriate funding and regulatory agencies. The investigator will apprise fellow investigators and study personnel of all adverse events that occur during the conduct of this research project [*describe how the investigator will meet with obligation, e.g., through regular study meetings, via email as they are reviewed by the principal investigator.*] [*Where appropriate, modify the following sentence to apply to the specific research protocol.*] The protocol's research monitor(s), e.g., industrial sponsor, Yale Cancer Center monitors, the Yale Center for Clinical Investigation Research Subject Advocates (YCCI RSAs), Cancer Center Protocol Review Committee (PRC), Quality Assurance and Compliance and Safety Committee (QUACS), DSMBs, study sponsors, funding and regulatory agencies, and regulatory and decision-making bodies will be informed of [*specify types of adverse events that require reporting to these oversight bodies*] adverse events within 5 days [*enter other appropriate duration*] of the event becoming known to the principal investigator.

Moderate Risk DSMP

1. Personnel responsible for the safety review and its frequency:

The principal investigator will be responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews at the specified frequency which must be conducted at a minimum of every 6 months (including when reapproval of the protocol is sought). During the review process, the principal investigator (monitor) will evaluate whether the study should continue unchanged, require modification/amendment, continue or close to enrollment. Either the principal investigator, the HIC or [*enter the names of other oversight bodies that have this authority, e.g., QUACS*] have the authority to stop or suspend the study or require modifications.

2. The risks associated with the current study are deemed moderate for the following reasons: (choose those that apply)

1. We do not view the risks associated with the _____ as minimal.
2. We do not view the risks associated with the combined use of _____ and _____ as minimal.
3. Given the now established safety and validity of the current _____ in our prior work, we do not view the proposed studies as high risk.
4. Given our experience with the combined co-administration _____, we do not view the proposed studies as high risk.

Although we have assessed the proposed study as one of moderate risk, the potential exists for anticipated and/or unanticipated adverse events, serious or otherwise, to occur since it is not possible to predict with certainty the absolute risk in any given individual or in advance of first-hand experience with the proposed study methods. Therefore, we provide a plan for monitoring the data and safety of the proposed study as follows:

3. Attribution of Adverse Events:

Adverse events will be monitored for each subject participating in the study and attributed to the study procedures / design by the principal investigator (*Insert Investigator Name*) according to the following categories:

- a.) Definite: Adverse event is clearly related to investigational procedures(s)/agent(s).
- b.) Probable: Adverse event is likely related to investigational procedures(s)/agent(s).
- c.) Possible: Adverse event may be related to investigational procedures(s)/agent(s).
- d.) Unlikely: Adverse event is likely not to be related to the investigational procedures(s)/agent(s).
- e.) Unrelated: Adverse event is clearly not related to investigational procedures(s)/agent(s).

4. Plan for Grading Adverse Events:

The following scale will be used in grading the severity of adverse events noted during the study:

1. Mild adverse event
2. Moderate adverse event
3. Severe

5. Plan for Determining Seriousness of Adverse Events:

Serious Adverse Events:

In addition to grading the adverse event, the PI will determine whether the adverse event meets the criteria for a Serious Adverse Event (SAE). An adverse event is considered serious if it:

1. is life-threatening
2. results in in-patient hospitalization or prolongation of existing hospitalization
3. results in persistent or significant disability or incapacity
4. results in a congenital anomaly or birth defect OR
5. results in death
6. based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition, or
7. adversely affects the risk/benefit ratio of the study

An adverse event may be graded as severe but still not meet the criteria for a Serious Adverse Event. Similarly, an adverse event may be graded as moderate but still meet the criteria for an SAE. It is important for the PI to consider the grade of the event as well as its "seriousness" when determining whether reporting to the HIC is necessary.

6. Plan for reporting serious AND unanticipated AND related adverse events, anticipated adverse events occurring at a greater frequency than expected, and other unanticipated problems involving risks to subjects or others to the HIC.

The investigator will report the following types of adverse events to the HIC; a) serious AND unanticipated AND possibly, probably or definitely related events; b) anticipated adverse events occurring with a greater frequency than expected; and c) other unanticipated problems involving risks to subjects or others.

These adverse events or unanticipated problems involving risks to subjects or others will be reported to the HIC within 48 hours of it becoming known to the investigator, using the appropriate HIC forms found on the website.

7. Plan for reporting adverse events to co-investigators on the study, as appropriate the protocol's research monitor(s), e.g., industrial sponsor, Yale Center for Clinical Investigation Research Subject Advocates (RSAs), Cancer Center's Quality Assurance, Compliance and Safety Committee (QUACS) Protocol Review Committee (PRC), DSMBs, study sponsors, funding and regulatory agencies, and regulatory and decision-making bodies.

For the current study, the following individuals, funding, and/or regulatory agencies will be notified: (choose those that apply)

- i. All Co-Investigators listed on the protocol.
- ii. **Yale Center for Clinical Investigation Research Subject Advocates (RSAs)**
- iii. Quality Assurance and Compliance and Safety Committee (QUACS)
- iv. National Institutes of Health
- v. Food and Drug Administration (Physician-Sponsored IND # _____)
- vi. _____ Medical Research Foundation (Grant _____)

The principal investigator (*Insert Investigator Name*) will conduct a review of all adverse events upon completion of every study subject. The principal investigator will evaluate the frequency and severity of the adverse events and determine if modifications to the protocol or consent form are required.

High Risk DSMP

(Please note: in addition to a DSMP, a DSMB will likely be required)

1. Personnel responsible for the safety review and its frequency:

The principal investigator will be responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews at the specified frequency which must be conducted at a minimum of every 6 months (including when reapproval of the protocol is sought). During the review process, the principal investigator (monitor) will evaluate whether the study should continue unchanged, require modification/amendment, continue or close to enrollment. Either the principal investigator, the HIC or [*enter the names of other oversight bodies that have this authority, e.g., QUACS*] have the authority to stop or suspend the study or require modifications.

2. The risks associated with the current study are deemed high for the following reasons: (choose those that apply)

1. We do not view the risks associated with the _____ as minimal/moderate.
2. We do not view the risks associated with the combined use of _____ and _____ as minimal/moderate.
3. Given the now established safety and validity of the current _____ in our prior work, we do not view the proposed studies as minimal/moderate.
4. Given our experience with the combined co-administration _____, we do not view the proposed studies as minimal/moderate.

Since it is not possible to predict with certainty the absolute risk in any given individual or in advance of first-hand experience with the proposed study methods, we provide a plan for monitoring the data and safety of the proposed study as follows:

3. Attribution of Adverse Events:

Adverse events will be monitored for every subject participating in the study and attributed to the study procedures / design by the principal investigator (*Insert Investigator Name*) according to the following categories:

- a.) Definite: Adverse event is clearly related to investigational procedures(s)/agent(s).
- b.) Probable: Adverse event is likely related to investigational procedures(s)/agent(s).
- c.) Possible: Adverse event may be related to investigational procedures(s)/agent(s).
- d.) Unlikely: Adverse event is likely not to be related to investigational procedures(s)/agent(s).

- f.) Unrelated: Adverse event is clearly not related to investigational procedures(s)/agent(s).

4. Plan for Grading Adverse Events:

The following scale will be used in grading the severity of adverse events noted during the study:

- 1 Mild adverse event
- 2 Moderate adverse event
- 3 Severe adverse event

5. Plan for Determining Seriousness of Adverse Events:

Serious Adverse Events:

In addition to grading the adverse event, the PI will determine whether the adverse event meets the criteria for a Serious Adverse Event (SAE). An adverse event is considered serious if it:

1. is life-threatening
2. results in in-patient hospitalization or prolongation of existing hospitalization
3. results in persistent or significant disability or incapacity
4. results in a congenital anomaly or birth defect OR
5. results in death
6. based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition, or
7. adversely affects the risk/benefit ratio of the study

An adverse event may be graded as severe but still not meet the criteria for a Serious Adverse Event. Similarly, an adverse event may be graded as moderate but still meet the criteria for an SAE. It is important for the PI to consider the grade of the event as well as its "seriousness" when determining whether reporting to the HIC is necessary.

6. Plan for reporting serious AND unanticipated AND related adverse events, anticipated adverse events occurring at a greater frequency than expected, and other unanticipated problems involving risks to subjects or others to the HIC.

The investigator will report the following types of adverse events to the HIC; a) serious AND unanticipated AND possibly, probably or definitely related events; b) anticipated adverse events occurring with a greater frequency than expected; and c) other unanticipated problems involving risks to subjects or others.

These adverse events and unanticipated problems involving risks to subjects or others will be reported to the HIC within 48 hours of it becoming known to the investigator, using the appropriate HIC forms found on the website.

7. Plan for reporting adverse events to co-investigators on the study, as appropriate the protocol's research monitor(s), e.g., industrial sponsor, Yale Cancer Center monitors, the Yale Center for Clinical Investigation (YCCI) Research Subject Advocates (RSAs), Cancer Center's Quality Assurance, Compliance and Safety Committee (QUACS), DSMBs, study sponsors, funding and regulatory agencies, and regulatory and decision-making bodies.

For the current study, the following individuals, funding, and/or regulatory agencies will be notified:

- i. All Co-Investigators listed on the protocol.
- ii. Yale Center for Clinical Investigation (YCCI) Research Subject Advocates (RSAs)
- iii. Quality Assurance and Compliance and Safety Committee (QUACS)
- iv. National Institutes of Health
- v. Food and Drug Administration (Physician-Sponsored IND # _____)
- vi. Medical Research Foundation (Grant _____)

The principal investigator (*Insert Investigator Name*) will conduct a review of all adverse events upon completion of every study subject. The principal investigator will evaluate the frequency and severity of the adverse events and determine if modifications to the protocol or consent form are required.

For more guidance on Adverse Event reporting and DSMP see http://oscar.med.yale.edu/hsp/module_6/4_guidance.asp