1. BACKGROUND:

The Dana-Farber/Harvard Cancer Center's (DF/HCC) Data and Safety Monitoring Committee (DSMC) is charged with providing ongoing monitoring for high-risk Pilot, Phase I and Phase II clinical trials initiated and conducted by DF/HCC investigators. The primary purpose of the committee is to ensure the safety of study participants as well as evaluate the overall progress of the trial.

2. ASSOCIATED DF/HCC POLICIES:

2.1. COM-100
2.2. DATA-100

3. PROCEDURE:

3.1. Protocols Requiring Monitoring:

3.1.1. The Scientific Review Committees (SRC and PSRC), Institutional Review Board (IRB) and/or the Clinical Investigations Leadership Committee (CLC) will identify high-risk DF/HCC initiated protocols.

3.1.1.1. High Risk protocols include, but are not limited to:

- DF/HCC investigator-sponsored interventional trials, DF/HCC multi-center trials, DF/HCC held IND/IDE trials
- First in human and/or pediatric clinical trials that do not have an established DSMC
- Gene transfer protocols that do not have an established DSMC
- Vaccine trials using live or attenuated viruses that do not have an established DSMC
- Other unusually complex or intensive protocols requiring a DSMC as determined by the SRC, PSRC, IRB and/or CLC

3.1.1. High-risk externally sponsored trials must have a designated DSMC or appropriate Data and Safety Monitoring plan in place. The DFCI IRB may require additional documentation from external sponsors to ensure the oversight is appropriate. The DF/HCC DSMC will not act as the oversight committee for trials under a non-DF/HCC regulatory sponsor. However, if directed by the SRC, IRB and/or CLC, the DF/HCC DSMC may monitor the local conduct *only* for high-risk externally-sponsored protocols.

3.2. Protocol Review Procedures:

3.2.1. The DSMC meets monthly to review toxicity, data submission compliance and accrual. Protocols are typically reviewed every 3, 6 or 9 months based on the protocol status, accrual rate, and review

of ongoing safety indicators.

3.2.2. ODQ notifies the ~~Overall PI~~sponsor-investigator and ~~lead study team~~designated sponsor personnel of the next upcoming DSMC review for a given protocol. Notifications are typically sent 4-6 weeks prior to the scheduled review date.

3.2.3. The ~~Overall Principal Investigator (PI)~~sponsor-investigator, or designee, will submit the following to ODQ to facilitate review by the DSMC:

- Completed DSMC Monitoring Form
- DSMC Data and Missing Forms Report
- Multi-Center Progress Report (attached to DSMC Monitoring Form, for investigator-sponsored, multi-center trials only)

3.2.4. In addition, ODQ will prepare the following information to facilitate review by the DSMC:

- Protocol Summary and Registration Report
- OHRS Summary Report

3.2.5. The ~~Overall PI~~sponsor-investigator is responsible for data compliance of all participating sites both within and outside DF/HCC for ~~PI-Initiated~~investigator-sponsored research. The DF/HCC DSMC has the prerogative to review data submission compliance at any time, regardless of the next scheduled review.

3.2.5.1. The DSMC defines data submission compliance as less than or equal to 10% of total forms missing for both overall protocol compliance and site-specific compliance. Toxicity reporting, as a sub-category of missing forms, will also be held to the less than or equal to 10% threshold for site-specific compliance.

3.2.5.2. In the event the percentage of total missing forms or site-specific toxicity forms is greater than 10%, but the total of number of forms missing is small, the DSMC Chair has the discretion to deem the protocol compliant.

3.2.6. When protocols are identified as non-compliant with data submission, the following procedures, dependent on the percentage of missing forms, will be followed.

3.2.6.1. If a protocol has > 10% but ≤20% of total forms missing for the overall protocol or toxicity forms missing at any one site:

3.2.6.1.1. Notice of percentage of forms missing and a reminder of data submission compliance criteria will be incorporated into the DSMC response memos.

3.2.6.1.2. The protocol will be given a 3-month review. At the time of the 3-month review:

3.2.6.1.2.1.If the protocol data ~~is~~ are compliant, the protocol will be assigned its next review date based on DSMC recommendation of the safety review.

3.2.6.1.2.2.If the protocol remains non-compliant, an email memo will be sent no later than the next business day to the ~~Sponsor, Overall PI, Site Responsible Investigator~~sponsor-investigator ~~(if applicable)~~, designated research team member and applicable clinical trials office defining deadlines for data submission compliance and consequences for failure to comply. Data must be compliant (<10% of total forms missing and <10% of site specific toxicity forms missing) within 2 weeks after the DSMC meeting.

3.2.6.2.If the protocol has >20% of total forms missing for the protocol or toxicity forms missing at any one site:

3.2.6.2.1. An email memo will be sent no later than the next business day (Monday – Friday) to the ~~Sponsor, Overall PI, Site Responsible Investigator (if applicable)~~sponsor-investigator, designated ~~research team member~~sponsor personnel, and applicable clinical trials office defining deadlines for data submission compliance and consequences for failure to comply. Data must be compliant (<10% of forms missing) within 2 weeks after the DSMC meeting.

3.2.6.3.If a 2-week data compliance deadline is not met, the following actions will be applied:

3.2.6.3.1. For protocols open to accrual where the overall % of missing forms is out of compliance, accrual will be suspended at **ALL** sites. On behalf of the DSMC, ODQ will submit a c~~C~~losure to a~~A~~ccrual ~~form~~ request to the Institutional Review Board (IRB).

3.2.6.3.2. For protocols open to accrual where a specific site(s) is out of compliance, accrual will be suspended at the specific site(s). On behalf of the DSMC, ODQ will submit a c~~C~~losure to a~~A~~ccrual ~~form~~ request to the Institutional Review Board (IRB).

3.2.6.3.3. For protocols already closed to accrual, the ODQ DSMC coordinator will send a memo to the Director of the Office for Human Research Studies (OHRS) recommending suspension of activity on any pending protocols of the ~~Sponsor, Overall PI and/or Site Responsible Investigator~~sponsor-investigator ~~where applicable~~.

3.2.6.4.No data analysis, abstract or publication may take place while a protocol is out of data compliance.

3.2.6.5.The DSMC Chair has the discretion to adjust the timeframes listed above.

3.3. **Committee Membership and Meeting Logistics**

3.3.1. Committee members are appointed by the Senior VP for Research and will include at a minimum:

Voting Members:

- [3] Medical Oncologists (including the committee Chair)
- [1] ad hoc Physician as needed (Radiation Oncologist, Surgeon, etc)
- [1] Biostatistician
- [1] Nurse
- [1] Pharmacist

Non-voting Member:

- [1] Meeting Coordinator

3.3.2. ODQ will maintain DSMC meeting minutes and correspondence. DSMC recommendations made to study teams and reported to the IRB and the Clinical Investigations Leadership Committee (CLC). A summary of all DSMC activity is reviewed by CLC monthly.

3.3.3. All trial and participant information will remain confidential. All DSMC members are required to sign a Confidentiality and Conflict of Interest (COI) Statement related to the trials discussed. Members will recuse themselves from the discussion and voting if a conflict exists for a given protocol.