1.0 Purpose:

1.1 The federal regulations stipulate that the IRB must determine that: "When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects."

1.2 The purpose of this policy is to describe the requirements for and elements of a Data and Safety Monitoring Plan (DSMP) for human subjects research protocols conducted by Hartford HealthCare (HHC) investigators. The purpose of the DSMP is to promote subject safety and to protect study integrity and validity. Therefore, the Hartford HealthCare Institutional Review Board (HHC IRB) will take the DSMP into consideration when determining whether the study meets the criteria for approval.

2.0 Definitions:

2.1 **Data and Safety Monitoring Plan (DSMP)** - A plan or strategy, tailored to a particular protocol that is used to assess the assumptions made in the study protocol and ensure continued safety and welfare of human subjects.

2.2 **Risk Categories** associated with participating in a study**:**

2.2.1.1 **Minimal Risk** - Risk commensurate with ordinary daily life or with risks encountered in the performance of routine physical or psychological examinations. Examples may include blood draws of small volumes for research purposes, the collection of biological specimens for research purposes by noninvasive means, the collection of data from medical records, and most research employing surveys, interviews, or focus groups.

2.2.1.2 **Greater than minimal risk (High)** – Risk that in terms of potential harm to a subject is high because of the nature of the study or because there is significant uncertainty about the possible occurrence or nature of the risks. Examples include most Phase I drug trials.

2.3 **Adverse Event** - An undesirable and unintended, although not necessarily unexpected, result of therapy or other intervention.

2.4 **Unanticipated Event** - Unanticipated events are risks/events which are not cited in the protocol, the consent form or the Investigator's Brochure.

2.5 **Related Event -** An event is "related" if it is possibly, probably, or definitely caused by the research procedures.

2.6 **Serious Adverse Event** - Any adverse event that results in any of the following outcomes: death, a life-threatening experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect, or any other adverse event that, 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.

2.7 **Unanticipated Problems Involving Risks to Subjects or Others -** Any incident, experience or outcome that (a) is unexpected (in terms of nature, severity, or frequency) given the research procedures described in the protocol and the characteristics of the subject population and (b) suggests that the research participation places or has the potential to place subjects at greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized and (c) is related or possibly related to participation in the research.

2.8 **Data and Safety Monitoring Board (DSMB)/Data Monitoring Committee (DMC) –** A formal committee that is established specifically to monitor data throughout the life of a study to determine if is appropriate, from both a scientific and ethical standpoint, to continue the study as planned.

2.9 **Stopping rules** – Pre-determined guidelines that are used to determine that the study should be altered or stopped, based on review of study related events that occur during the conduct of the study.

3.0 Procedure:

3.1 Data Safety and Monitoring is the process for systematically reviewing accumulated outcome data from an ongoing research study to ensure the continuing safety of current participants and those yet to be enrolled, as well as an effort to ensure the continuing validity and scientific merit of the research study.

3.2 A Data Safety and Monitoring Plan (DSMP) should be tailored to the nature, size, and complexity of the research protocol, the expected risks of the research, and the type of subject population being studies. Appropriate DSMPs may fall anywhere along a continuum from monitoring by the Principal Investigator or group of investigators to the establishment of an independent Data and Safety Monitoring Board (DSMB).

3.3 A Data Safety Monitoring Plan is required for:

- 3.3.1 All studies considered greater than minimal risk
- 3.3.2 Multi-site research where HHC is the coordinating site
- 3.3.3 Studies where there is an NIH or FDA requirement for a plan
- 3.3.4 Studies when requested by the IRB

3.4 Plans should address at least the following elements:

- 3.4.1 Identify who will be responsible for monitoring the data collected, including data related to unanticipated problems and adverse events, and their respective roles (e.g., the investigators, the research sponsor, a coordinating or statistical center, an independent medical monitor, a DSMB/DMC, and or some other entity).

- 3.4.2 Procedures (e.g. lab tests, evaluations, observations and their frequency) which will be utilized to monitor subject safety and confidentiality of data.

3.4.3 The time frames for reporting adverse events and unanticipated problems to the monitoring entity, such as the research sponsor, coordinating or statistical center, independent medical monitor, or DSMB/DMC.

3.4.4 The frequency of assessments of data or events captured by the monitoring plan, such as points in time or after a specific number of participants are enrolled.

3.4.5 As appropriate, procedures for communicating to the IRB, the study sponsor, and other appropriate entities the outcome of the reviews by the Monitoring Entity.

3.4.6 Stopping rules which define critical thresholds for stopping or modifying the study.

3.5 **When is a DSMB/DMC Required?**

3.5.1 The IRB may, in certain circumstances, require a DSMB depending on the level of risk or if there is a potential for a significant conflict of interest.

3.5.2 A DSMB/DSMC may be appropriate:

3.5.2.1 In any study where the risk level is greater than minimal (high)k especially those involving highly toxic therapies
3.5.2.2 Large subject numbers where risk may be better assessed through statistical comparisons between treatment groups
3.5.2.3 High expected rates of morbidity and mortality in the study population
3.5.2.4 When a HHC Principal Investigator (PI) holds the IND for the investigational agent being used in the study.
3.5.2.5 For multiple site studies, since it may be more difficult to recognize a pattern of increased or unusual problems when investigators treat small fractions of the population separately.
3.5.2.6 For Phase I and II trials if the studies have multiple clinical sites, are blinded, or employ particularly high-risk interventions or enroll vulnerable populations.
3.5.2.7 When HHC is the coordinating site of a multicenter study.
3.5.2.8 As a mechanism of managing a real or potential Conflict of Interest.

3.5.3 When a DSMB is involved, the DSMB's organization, membership, responsibilities and operations should be described. Membership should include individuals with expertise in the field, experience in the conduct of clinical trials, and or statistical expertise.

3.5.4 The DSMB generally should be independent from the sponsor and investigator team. Members should not have any serious conflicts of interest, such as financial interests that could be substantially affected by the outcome of the trial, strong views on the relative merits of the interventions under study, or relationship with the sponsor or those in

trial leadership positions that could be considered reasonably likely to affect their objectivity

3.5.5 The DSMB should be responsible for reviewing comprehensive, cumulative, unblinded safety reports, and employing stopping rules if there is evidence of differential effects in either risk or benefit. The descriptions of standard operating procedures should include frequency and documentation of periodic reviews, and submittal of written summary or minutes to the principal investigator.

3.5.6 When the HHC PI is required by the HHC IRB to constitute a DSMB, the following will be required:

3.5.6.1 All DSMB members, or the majority of DSMB members do not have HHC appointments.

3.5.6.2 DSMB members do not have interests, financial or otherwise, in the outcome of the study.

3.5.6.3 DSMB members who may be internal to HHC do not have reporting relationships to members of the research team.

3.5.6.4 DSMB members who are internal to HHC are not members of the same department or section as the HHC PI.

3.5.7 The investigator, upon receipt, must submit the DSMB findings and recommendations to the IRB.

3.6 The HHC IRB will assess the adequacy of the proposed Data and Safety Monitoring Plan during its review of a protocol, and may require that a DSMB be established for the study, as a condition necessary for the IRB's final approval.

3.7 When DSMBs are utilized, the HHC IRB may rely on a current statement from the DSMB indicating that it has and will continue to review study-wide Adverse Events, interim findings, and any relevant literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB.

4.0 Documentation:

4.1 The HHC HRPP office will maintain all records related to the implementation of this policy, electronic communications and notifications to investigators, funding or regulatory agencies, etc.

4.2 Records will be archived for a period of at least six (6) years following the termination or completion of the research activities.

5.0 References:

5.1 45 CFR 46.111(a)(6)

5.2 21 CFR 56.111(a)(6)

5.3 National Institutes of Health (NIH) Policies and Institutes and Centers (IC) Guidance for Data and Safety Monitoring of Clinical Trials - https://grants.nih.gov/policy/humansubjects/policies-and-regulations/data-safety.htm

5.4 Institutional Review Board Management and Function, Bankert, E. A., Amdur, R. J., 2nd Edition, 2006

6.0 Revision History:

Rev #	Initials	Effective Date	Description of Change(s)
00	CLG	7/1/11	New Issue
01	CLB	3/15/20	General review. Update reference link.

Element II.3.B and III.1.C.