Re-envisioning Memorial Sloan Kettering Cancer Center's Data and Safety Monitoring Committee

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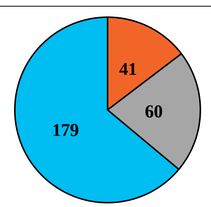
Background

- Memorial Sloan Kettering Cancer Center's (MSK) Data and Safety Monitoring Plan includes two institutional committees—the Data and Safety Monitoring Committee (DSMC) for non-phase 3 trials and the Data and Safety Monitoring Board (DSMB) for phase 3 randomized trials.
- These committees are essential for cancer centers like MSK, whose active portfolio includes over 800 clinical research protocols.
- In 2017, MSK created the Protocol Review Core (PRC) that provides centralized oversight and administration of MSK's protocol review committees, including DSMC and DSMB.
- DSMC and DSMB were centralized through PRC to optimize previously siloed processes. Based on portfolio size, PRC prioritized streamlining DSMC's processes and identified several areas for improvement.
- DSMC's current portfolio consists of 280 protocols, 266 of which are MSK Investigator Initiated Trials (IITs). Figure 1 outlines the portfolio by risk level.

Figure 1: DSMC Portfolio by Risk Level



Goals

- Clarify monitoring criteria to appropriately identify protocols requiring DSMC oversight
- Update review processes
- Leverage technology to better coordinate DSMC reviews

Changes Implemented

	BEFORE	AFTER
Mission & Focus	• Not clearly defined. • Focused on study progress and accrual.	• Focus on safety (unanticipated or excessive toxicity, protocol-specific stopping rules), data (completeness, accuracy, and database integrity), and progress and accrual.
Review Frequency	• Quarterly meetings. • Risk-based monitoring (high=quarterly, moderate=biannually, low=annually).	• Added ad hoc meetings for flexibility. • Risk-based monitoring is unchanged. • Low risk focus is on interventional protocols.
Review Criteria	• Monitored trials when external monitoring was less frequent than every 6 weeks.	• Eliminated overlap with external monitoring. ○ Eligible: MSK IITs and external protocols for which MSK is the data coordinating center. ○ Ineligible: retrospective, biospecimen, specimen banking, and external protocols.
Protocol Identification	• Local study teams & DSMC identified eligible protocols once opened to accrual (OTA).	• Simplified identification of eligible protocols. • Protocol Review Core identifies eligible protocols once OTA.
Monitoring Life Cycle	• Monitoring initiated once a protocol OTA. • Monitoring ends once closed to accrual (CTA).	• Monitoring initiated following 1st accrual or 1 year after OTA if no accruals. • Monitoring continues until no active participants.
Submission Requirements	• DSMC Monitoring Form had limited open-ended questions and lacked flexibility for the different types of trials.	• DSMC monitoring form revamped with questions to help identify potential issues. PI must provide more detail on matters such as serious adverse events, interim analyses, audits, etc. • Protocol Review Core created tools to aid study teams in providing complete submissions.
Statistical Reviews	• DSMC statistician did not conduct formal reviews.	• Incorporated routine statistical reviews to evaluate stopping rules, interim analyses, amendment trends, etc.
Reviewer Checklist	• Reviewer checklist was vague and lacked focus.	• Updated reviewer checklist to ensure focus, detail, and consistency across reviews (Figure 2).
Reviewer Education & Experience	• Limited to onboarding process.	• Incorporated ongoing educational presentations into DSMC meetings. • Initiated member surveys to improve engagement and satisfaction.
Inter-committee Communication	• Infrequent communication between the DSMC and other institutional committees.	• Increased communication with committees such as Institutional Review Board (IRB) and Protocol Review and Monitoring System (PRMS).
Leveraging Institutional Technology	• Used MSK's home-grown web-based application called Protocol Information Management System (PIMS) for reviews, meeting minutes, and review letters. • Submissions via email.	• Enhanced PIMS to improve identification of eligible protocols, enable electronic submissions, optimize tracking, and allow for expedited reviews. • Implemented inclusion of IRB/PRMS documents for DSMC reference within centralized review tab (Figure 3).

Figure 2: PIMS Reviewer Checklist

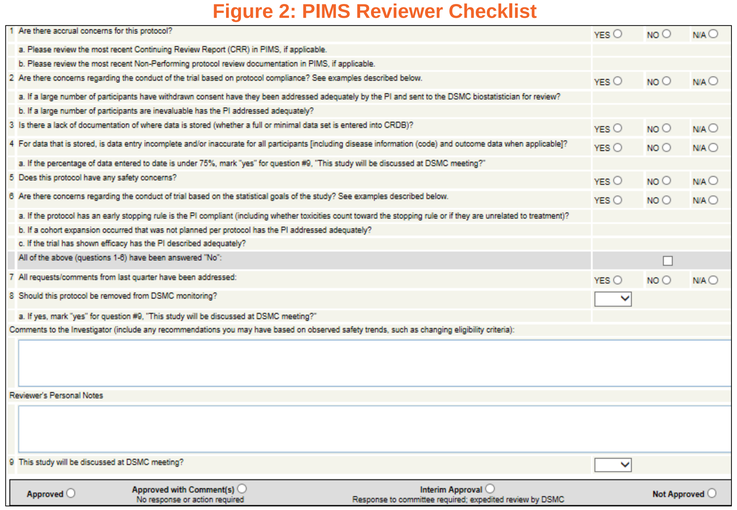
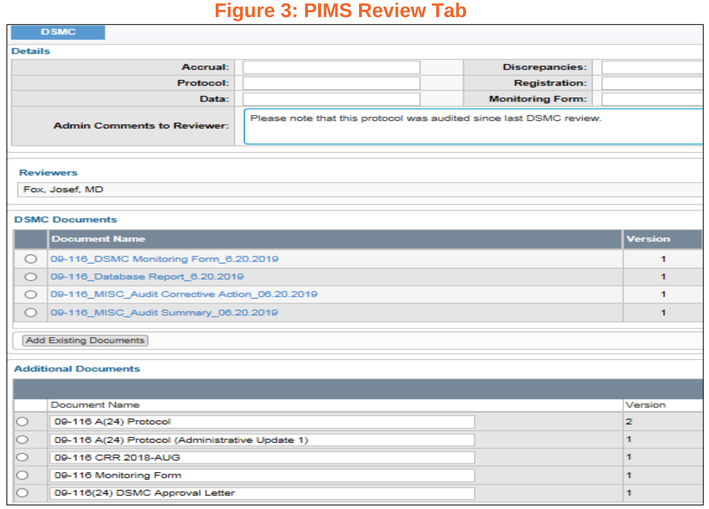


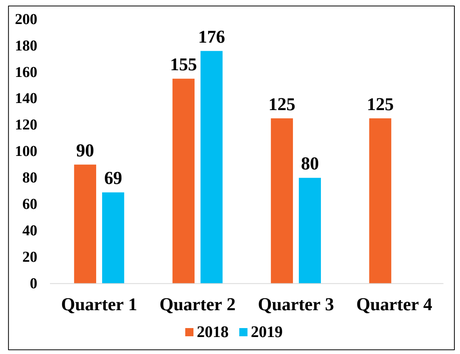
Figure 3: PIMS Review Tab



Outcomes

- Simplified submission and review workflows are more efficient.
- Transparency has improved amongst DSMC and other institutional committees.
- For quarters 1-3, 2019 volume has decreased 12% compared to 2018 due to thoughtful monitoring criteria.
- 495 reviews were conducted in 2018 and 325 have been conducted in 2019 to date for quarters 1-3 (Figure 4).
- The decreased volume ensures reviewers can conduct efficient, comprehensive reviews.

Figure 4: DSMC Volume, 2018-2019



Conclusions

- The committee functions as an institutional service to investigators and study teams.
- DSMC communicates with IRB and PRMS for adequate portfolio management with minimal overlap.
- Processes, review requirements, and resources are clear and transparent.

Future Directions

- Streamline submission data requirements
- Incorporate data visualization
- Implement a DSMC charter and SOPs
- Additional PIMS enhancements
- Create educational materials