# An Approach to Revitalizing PRMS Scientific Progress Reviews

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## BACKGROUND

National Cancer Institute (NCI) Cancer Center Support Grant (CCSG) Guidelines call for a mechanism for assuring adequate internal oversight of the scientific aspects of cancer trials. The Protocol Review and Monitoring System (PRMS) has the authority to terminate protocols that do not demonstrate scientific progress. Yale Cancer Center (YCC) PRMS had a process in place whereby demonstration of scientific progress was determined based upon biannual presentations by the Disease Aligned Research Team (DART). The DART Leader presented the portfolio to the Protocol Life Cycle Subcommittee (PLCS) of the Protocol Review Committee (PRC), a component of Yale's PRMS. It was logistically challenging to coordinate the presentation of 14 DARTs biannually. As a result, DART presentations were infrequent and evaluation of protocols was primarily based upon low accrual.

## AIMS

To develop a robust process for consistent reviews of scientific progress in an expedited and structured manner while minimizing the burden on the DART Leaders and PLCS members.

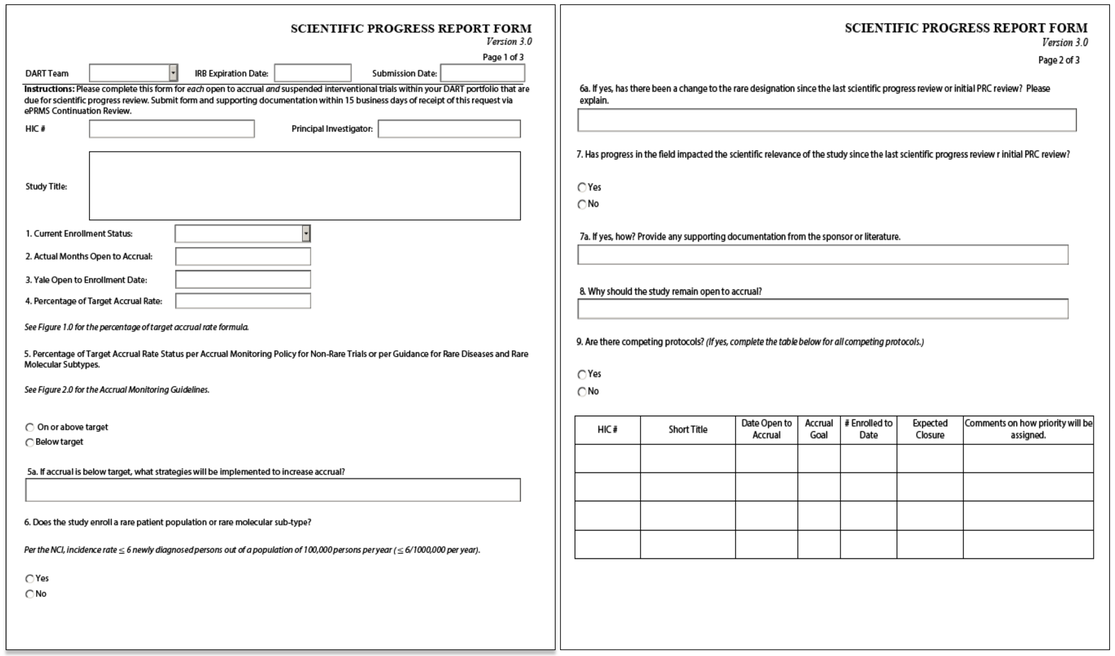
## METHODS

PLCS staff developed and implemented a revised process for scientific progress reviews. PLCS evaluates the scientific progress of interventional trials that are open to accrual or temporarily suspended at the time of IRB renewal. Trials that are not scientifically relevant or will not meet their scientific objective(s) may be recommended to the PRC for closure.

We outlined the policy and procedures for scientific progress reviews, developed submission (Figure 1) and reviewer forms (Figure 2) and submission instructions. We utilized the ePRMS Console of Yale School of Medicine's Clinical Trials Management System, OnCore, for submission. We generated reports within OnCore to determine which studies are due for submission.

We educated and trained the research teams, PRMS members and PRMS staff on the process, communicated with key stakeholders, and announced the implementation plan.

**Figure 1.**



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DART Team: IRB Expiration Date: Submission Date:

**Instructions:** Please complete this form for *each* open to accrual and suspended interventional trials within your DART portfolio that are due for scientific progress review. Submit form and supporting documentation within 15 business days of receipt of this request via ePRMS Continuation Review.

HIC # Principal Investigator:

Study Title:

1. Current Enrollment Status:
2. Actual Months Open to Accrual:
3. Yale Open to Enrollment Date:
4. Percentage of Target Accrual Rate:

*See Figure 1.0 for the percentage of target accrual rate formula.*

5. Percentage of Target Accrual Rate Status per Accrual Monitoring Policy for Non-Rare Trials or per Guidance for Rare Diseases and Rare Molecular Subtypes.

*See Figure 2.0 for the Accrual Monitoring Guidelines.*

○ On or above target
○ Below target

5a. If accrual is below target, what strategies will be implemented to increase accrual?

6. Does the study enroll a rare patient population or rare molecular sub-type?

*Per the NCI, incidence rate ≤ 6 newly diagnosed persons out of a population of 100,000 persons per year (≤ 6/1000,000 per year).*

○ Yes
○ No

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6a. If yes, has there been a change to the rare designation since the last scientific progress review or initial PRC review? Please explain.

7. Has progress in the field impacted the scientific relevance of the study since the last scientific progress review r initial PRC review?

○ Yes
○ No

7a. If yes, how? Provide any supporting documentation from the sponsor or literature.

8. Why should the study remain open to accrual?

9. Are there competing protocols? *(If yes, complete the table below for all competing protocols.)*

○ Yes
○ No

| HIC # | Short Title | Date Open to Accrual | Accrual Goal | # Enrolled to Date | Expected Closure | Comments on how priority will be assigned. |
|---|---|---|---|---|---|---|
| | | | | | | |
| | | | | | | |
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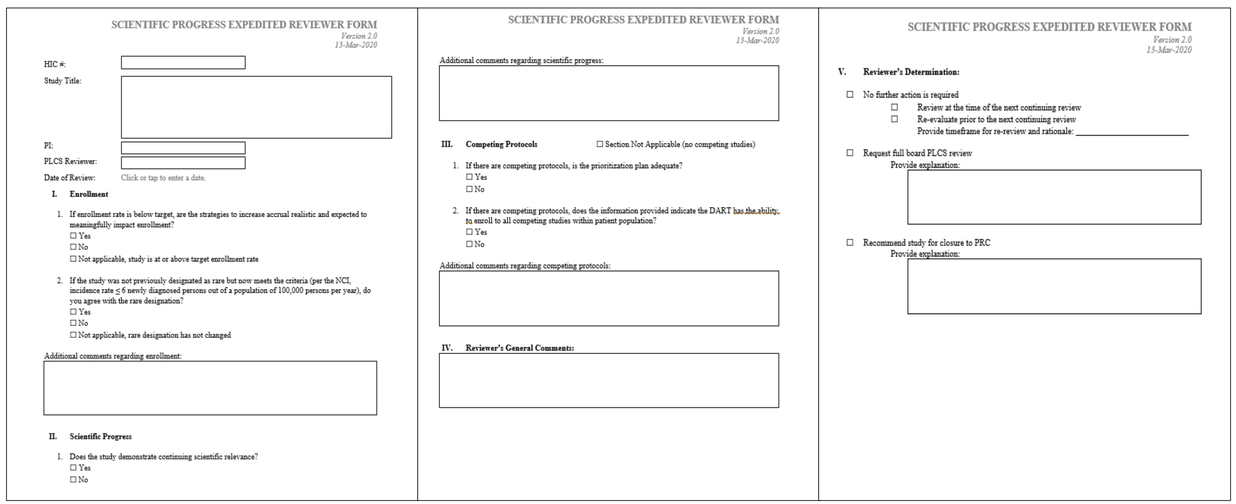
**Figure 2.**



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*13-Mar-2020*

HIC #:
Study Title:
PI:
PLCS Reviewer:
Date of Review: Click or tap to enter a date.

**I. Enrollment**

1. If enrollment rate is below target, are the strategies to increase accrual realistic and expected to meaningfully impact enrollment?
   ☐ Yes
   ☐ No
   ☐ Not applicable, study is at or above target enrollment rate
2. If the study was not previously designated as rare but now meets the criteria (per the NCI, incidence rate ≤ 6 newly diagnosed persons out of a population of 100,000 persons per year), do you agree with the rare designation?
   ☐ Yes
   ☐ No
   ☐ Not applicable, rare designation has not changed

Additional comments regarding enrollment:

**II. Scientific Progress**

1. Does the study demonstrate continuing scientific relevance?
   ☐ Yes
   ☐ No

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Additional comments regarding scientific progress:

**III. Competing Protocols** ☐ Section Not Applicable (no competing studies)

1. If there are competing protocols, is the prioritization plan adequate?
   ☐ Yes
   ☐ No
2. If there are competing protocols, does the information provided indicate the DART has the ability to enroll to all competing studies within patient population?
   ☐ Yes
   ☐ No

Additional comments regarding competing protocols:

**IV. Reviewer's General Comments:**

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**V. Reviewer's Determination:**

☐ No further action is required
   ☐ Review at the time of the next continuing review
   ☐ Re-evaluate prior to the next continuing review
   Provide timeframe for re-review and rationale: _____
☐ Request full board PLCS review
   Provide explanation:
☐ Recommend study for closure to PRC
   Provide explanation:

## RESULTS

DART portfolio reviews were presented annually in 2015-2017 despite the expectation for biannual presentation. In 2016, three of 14 DARTs did not present and in 2018, 13 DARTs did not present their portfolios, which prompted suspension of portfolio reviews in Jun-2018. Since Oct-2019 when the new process was implemented, 13 of 14 DARTs have had individual protocols reviewed.

We do not yet have sufficient data to demonstrate the impact of the process on the rate of closure due to lack of scientific progress.

## CONCLUSIONS

We encountered studies where closure to accrual was imminent and a review of scientific progress was not necessary. Submitters communicate the expected closure date, provide supporting sponsor correspondence and review is waived.

We faced system limitations in the ePRMS console. Submitters cannot create another review of a different type when a review is in progress. To resolve, we withdrew the scientific progress report to allow submission of another type (i.e., an amendment), then resubmitted the scientific progress report when the other review is complete.

We have experienced delays in submission. PLCS members are determining how to handle late submissions and the appropriate action after sufficient follow-up attempts are made.

We are considering using the IRB renewal report in lieu of a scientific progress report.