Inside the Data Monitoring Committee

Evolution, Myths, and Lessons Learned

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Disclaimer

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- IDMCs: Pfizer

Scope

While DMCs are utilized in a wide array of clinical trials, today's webinar will focus on those sponsored by industry

What is a Data Monitoring Committee?

- A DMC (or Data Safety Monitoring Board [DSMB]) is an **independent group** of experts (clinicians, statisticians, etc.)
- DMCs **periodically review data** from ongoing clinical trials to ensure patient safety, trial integrity, and validity of results
- DMCs **make recommendations** to continue, modify, or stop the trial based on risk-benefit assessments of their data review
- DMCs are **important for trials** with mortality and severe morbidity endpoints, “vulnerable” populations, and large and/or long-duration trials

Key functions of a DMC

- **Patient safety**: Monitor for adverse event signals of interest and overall well-being of the trial participants
  - Review ongoing efficacy summaries to put potential safety issues in context
- **Trial integrity**: Reviews protocol adherence and trial viability
- **Patient accrual**: Provides advice when accrual is lacking
- **Risk-benefit assessment**: Determines if the potential benefits still outweigh the risks of the trial
- **Recommendations**: Advises the sponsor on continuing, changing, or stopping the trial

When is a DMC needed?

- Trials that **utilize irreversible endpoints** (e.g., severe morbidity or mortality)
- Trials that **involve unusual or possible risks** related to the toxicity of the treatment or from the underlying disease
- When trials are **conducted among many investigator sites** over a long period of time
- When there is a **regulatory or IRB requirement** (e.g., trial conducted in an emergency setting)
- When clinical trials are **conducted in "vulnerable" populations** (e.g., pediatrics, pregnant women, immune-compromised patients)

Patient safety and trial integrity: Two sessions, same objective

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Aspect	Open DMC Session	Closed DMC Session
Participants	DMC members, sponsor representatives, support personnel, and select trial team members	Only DMC members and designated support personnel
Review Focus	Trial conduct, protocol adherence, data quality, and operational issues	Unblinded efficacy and safety data
Discussion Topics	Discuss emerging safety results at an aggregate level in a blinded manner	Benefit-risk balance and emerging trends
Value	Provides an opportunity for clarification and information exchange	Discusses concerns, differing viewpoints, and potential actions confidentially
Outcome	Preserves transparency while avoiding disclosure of treatment-specific interim results	Develops independent recommendations regarding trial continuation, modification, or termination

Pioneering the industry DMC model

Frank and Jay organized the first DMC for an industry-sponsored clinical trial in 1988

- What was happening at the time that made you realize a DMC was needed for this trial?
- What were the biggest hurdles you had to overcome?
- What lessons have stayed with you throughout your careers?

Let’s go inside the room

- For those who have never attended a DMC meeting, what would surprise them about what actually happens in the room?
- When you look back across all the DMCs you’ve served on, what’s an interesting challenge or controversy that you’ve dealt with?
- What’s a lesson from behind closed doors that every clinical trial professional should hear?

Persistent myths about DMCs

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Information

- X Should be blinded to treatment
- X Should only review safety data
- X Information must be complete and fully current
- X Must have rigid restrictions on information provided

Analyses

- X Must follow the SAP exactly
- X Monitoring boundaries must be implemented rigidly
- X Reports can be entirely preprogrammed
- X Reports must be based only on cleaned adjudicated data

Operations

- X Meetings must be scheduled precisely and limited in number
- X Members review each AE / SAE
- X Members should indemnify the sponsor
- X Recommendations require formal voting

What makes an effective DMC?

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DMC Chair

- ✓ Strong clinical trial expertise
- ✓ Independent and credible
- ✓ Sound judgment under uncertainty
- ✓ Facilitator and diplomat

DMC Member

- ✓ Active clinical trialist
- ✓ Expert scientific knowledge and judgment
- ✓ Commitment to patient safety
- ✓ Questioning and collaborative

Sponsor Representative

- ✓ Respect for DMC independence
- ✓ Puts patient welfare above the business
- ✓ Organizational influence
- ✓ Trusted and transparent
- ✓ Responsiveness

How sponsors can improve their support

- Allow the DMC Chair to run all meetings
- Be efficient in use of time for open sessions
- Be open-minded about DMC requests for additional programming
- Provide access to all needed data
- Utilize more talent than just “experienced” statistical members
- Consider using >1 statistician per DMC
- Take more care in contracting for SDAC services

SDAC = Statistical Data Analysis Center

Best practices for SDACs

- Create summary of safety data for members before meeting
- In addition to providing N for each treatment group, also report patient-years (PY) of exposure
- After approval by sponsor, create additional analyses requested by DMC
- Reporting statistician must be a statistician and not a programmer

How SDACs can improve their support

- Consider the DMC as your primary collaborator
- Produce more graphs
- Do not dump huge tables created for the NDA submission
- Appreciate the value of a good reporting statistician

Where are DMCs heading?

Rising demand for members due to growing number of DMCs:

- More complex designs like platform trials and program/asset-wide DMCs
- Many NIH-funded trials mandate them
- Regulatory agencies often recommend them for select trials
- Local investigator-initiated or single-site trials
- Regional networks
- Broad national or international trials

Also need new DMC members due to aging veterans

The call to action: Preparing the next generation

The gap between the demand and supply of trained DMC members is increasing

- Sponsors only want “experienced” members
- The cohort of “experienced” members is “actuarily challenged”
- Due to the advent of platform trials and multi-development platforms:
  - >1 statistician is often needed per DMC
  - New designs increase need for varied clinical expertise

I'm interested in serving on a DMC. What advice do you have for me?

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Here are some ideas:

- Access available training
- Phase 1 trials are a good introduction
- Get experience with internal DMCs (as available)
- Understand conflicts of interest
- Connect with us:

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Society for Clinical Trials resources

www.sctweb.org

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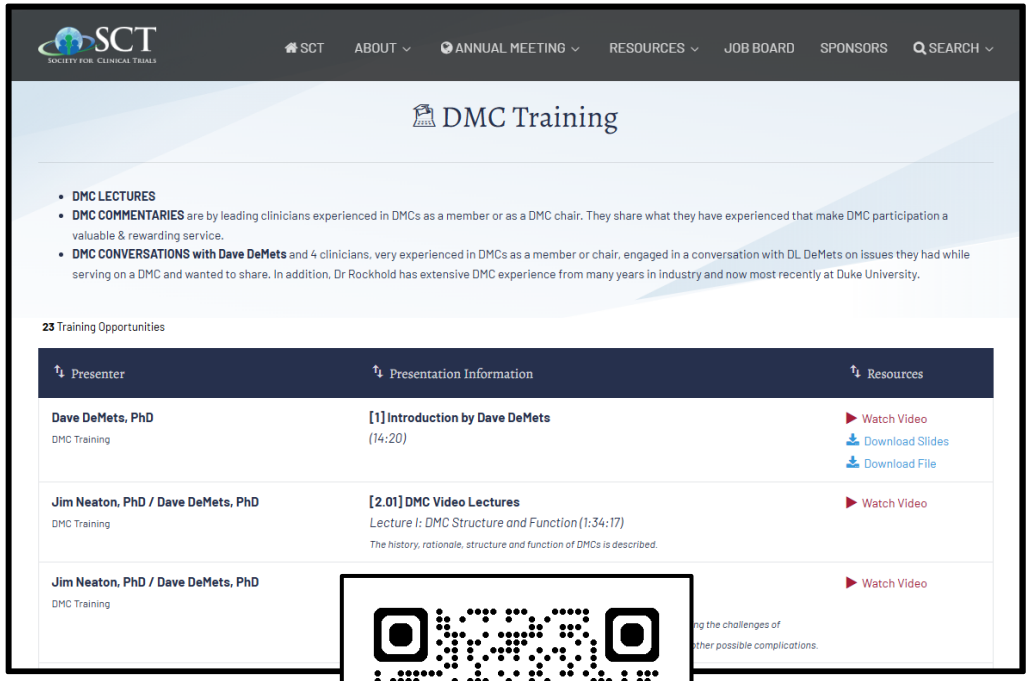
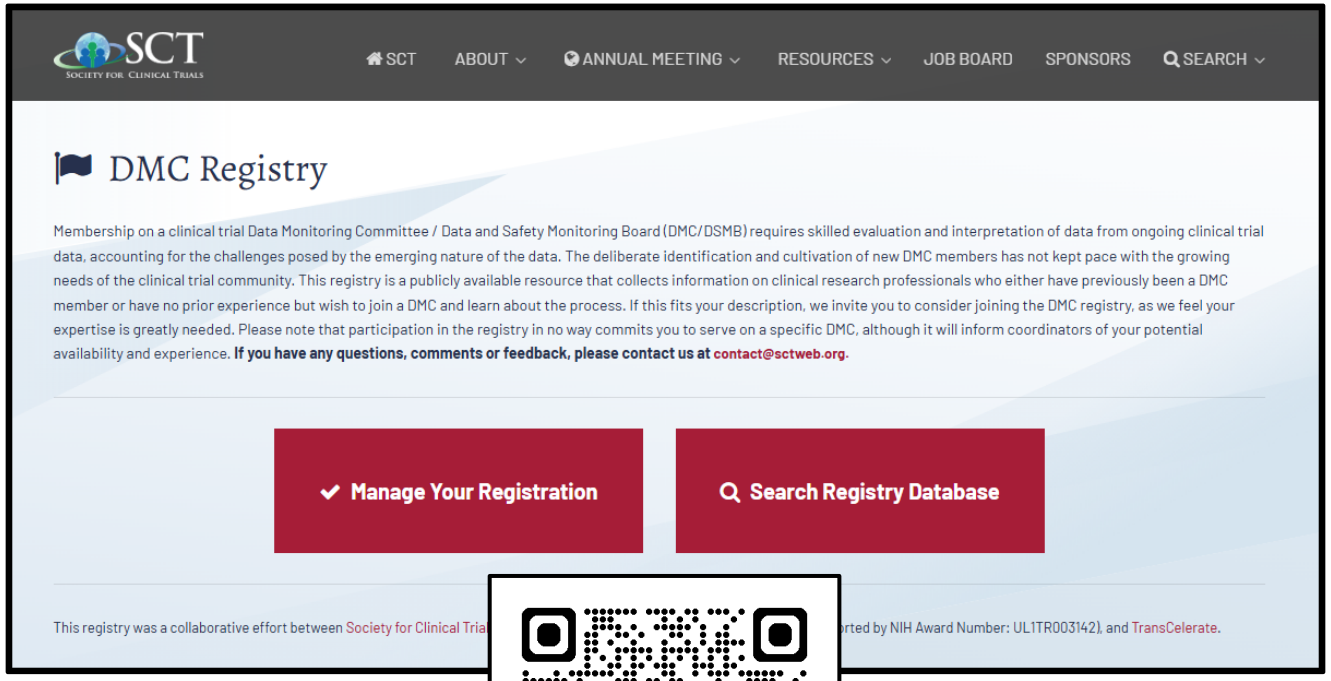
DMC training materials



DMC registry



Continue your learning

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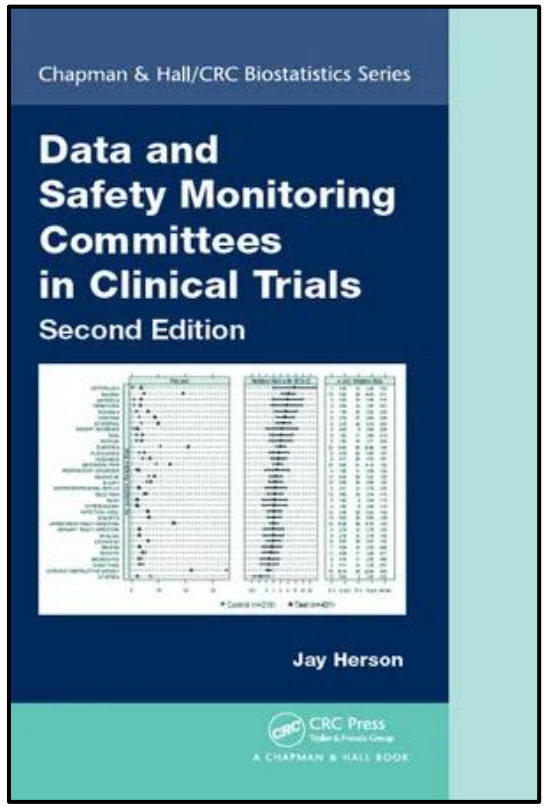

Foundational reference for best practices:

- Bridges the statistical, clinical, ethical, and operational aspects of DMC service
- Chapter Q&A with real-life examples

More info

Chapters:

- Introduction
- Organization of a Safety Monitoring Program for a Confirmatory Trial
- Meetings
- Clinical Issues
- Statistical Issues
- Bias and Pitfalls
- Data Monitoring Committee Decisions
- Emerging Issues

Selected other resources

- Calis KA, Archdeacon P, Bain R, DeMets D, Donohue M, Elzarrad MK, et al. Recommendations for data monitoring committees from the Clinical Trials Transformation Initiative. *Clin Trials*. 2017;14(4):342-348. doi:10.1177/1740774517707743.
- Fleming TR, Wittes J, Fiuzat M, Bristow MR, Rockhold FW, Connor JT, et al. Training the next generation of data monitoring committee members: an initiative of the Heart Failure Collaboratory. *JACC Heart Fail*. 2024;12(8). doi:10.1016/j.jchf.2024.02.016.
- Herson J, Ognibene FP, Peura DA, Silen W. The role of an independent data monitoring board in a clinical trial sponsored by a pharmaceutical firm. *J Clin Res Drug Dev.* 1992;6(4):285-292. link.
- Martin LF, Booth FV, Karlstadt RG, Silverstein JH, Jacobs DM, Hampsey J, et al. Continuous intravenous cimetidine decreases stress-related upper gastrointestinal hemorrhage without promoting pneumonia. *Crit Care Med.* 1993;21(1):19-30. doi:10.1097/00003246-199301000-00009.
- Rockhold FW, Mahaffey K, DeMets D. Training new DMC members: a call to action. *Ther Innov Regul Sci*. 2024;58:234-235. doi:10.1007/s43441-023-00580-8.

Selected other resources

- Wittes J, Barrett-Connor E, Braunwald E, Chesney M, Cohen HJ, DeMets D, et al. Monitoring the randomized trials of the Women's Health Initiative: the experience of the data and safety monitoring board. *Clin Trials*. 2007;4(3):218-234. doi:10.1177/1740774507079439.
- Xing X, Xing A, Natarajan K, Chu H, Lin L, Tong J. An alternative method for assessing the fragility of survival analysis results: a proof-of-concept study based on the log-rank test. *Am J Epidemiol*. 2026;195(4):1175-1181. doi:10.1093/aje/kwaf229.

Regulations:

- US Food and Drug Administration. Use of data monitoring committees in clinical trials: guidance for industry [Internet]. Silver Spring, MD: US Department of Health and Human Services; 2024 [cited 2026 Nov 01]. Available from: https://www.fda.gov/media/176107/download
- International Council for Harmonisation. ICH Topic E 9 Statistical principles for clinical trials [Internet]. Geneva: ICH; 2026 [cited 2026 Nov 01]. Available from: https://www.ema.europa.eu/en/scientific-guidelines/ich-e9-statistical-principles-clinical-trials

Q & A Session

Post-webinar note:
All questions submitted during the webinar are answered in the following slides by Dr. Rockhold and Dr. Herson. For questions answered live, please note that the written response may differ slightly from the response provided during the webinar. Please refer to the webinar recording for a full accounting.

Questions submitted during the webinar

Question:
On the topic of evolution, what are your thoughts on replacement of static reports (i.e. “fixed” [PDF] tables/figures) with dynamic/interactive reports (i.e. a web-based tool to interrogate the data)?

Answer:
Several software companies are working on this type of software, and we think we will see it coming into use. Also down the road are safety data collected from wearables. The new software will integrate these data to CRF safety data. The new software has already proven effective in detecting fraud. We don’t see DMC members using real time interactive reports for their main review, however, as it’s still custom to download and review the outputs offline. Interactive reports could be useful during the meeting to review data in real time though.

Questions submitted during the webinar

Question:
How is the composition (in terms of expertise) of a DMC determined (rigid requirements, or flexible rules of thumb)? What is the ideal composition of a DMC?

Answer:
In industry trials, one biostatistician and two MDs seems to be the standard these days. Consultants from specialties related to adverse events such as dermatologists, cardiologists, etc. are usually available on an ad hoc basis. The ideal would be more than one statistician per DMC, especially for program-wide and platform-trial DMCs.

Questions submitted during the webinar

Question:
Thanks for bringing DMCs to life. I'd love to be able to get involved. How can an experienced statistician, with no DMC experience, become a DMC statistician?

Answer:
We wish a person like yourself could just send in a CV to a sponsor and wind up on a DMC a few months later. Let's face it, this is a "who you know" industry. We would advise you to contact people you know at sponsors and CROs and indicate your interest. That seems to be the most effective way these days. Also, understand the concerns about conflict of interest.

Questions submitted during the webinar

Question:
How are DMCs better leveraging modern technology for learning about the safety story and characterizing safety topics of interest, such as using interactive safety graphics or AI agents?

Answer:
The DMCs use whatever technology the sponsor has provided. We suspect that these technologies will eventually appear. We have never been on a DMC where members have asked for new technologies. If we did, we would be turned down. The sponsor has their SOPs and only software that they have already vetted is used. The best situation is when the SDAC has good technology and you do not need to rely on the sponsor. In this case, the sponsor only needs to provide the data.

Questions submitted during the webinar

Question:
From a CRO with dedicated reporting statisticians, we often see sponsors propose tables and listings that we know are going to be thousands of pages in length. When we bring this up with sponsors and recommend more streamlined outputs (including graphs) for DMC members, we often get pushback that they want to provide the DMC members with ALL safety/lab data. Do you have a recommendation for how CROs could communicate better with sponsors that it is the desire of DMC members not to have tens of thousands of pages of outputs?

Answer:
The reason you are getting the thousand pages of output is because the sponsor has already paid for those thousand pages for the NDA and ISS. They don't want to incur any additional expense. Tell them that with the thousands of pages, the DMC will miss the poison mushroom because there are too many trees in the way. That should get their attention. This is another reason why the SDAC needs to be the driver of generating the output for what the DMC wants and needs.

Questions submitted during the webinar

Question:
How do you foster the partnership that is needed between the clinical and statistical scientist for learning about the safety topics of interest?

Answer:
As the biostatistical member of DMC, we have always had the respect of MD members and they have respected our statistical interpretations. If an MD were to say, “wait a minute, this is a clinical issue”, the best response is “there are no clinical issues, there are no statistical issues; only scientific issues and we all have a role in these”. An attitude like this should not be tolerated, as all DMC members are there for the patients.

Questions submitted during the webinar

Question:
What can the DMC do if a new safety topic of interest emerges and the existing set of analyses are inadequate for answering the new clinical questions?

Answer:
When this happens, we ask for more data, especially the narratives. We look more closely at the lab data than otherwise. We also ask for additional analyses. We have never been on a DMC where requests of this type have been turned down. Again, as in an earlier response, a skilled SDAC can provide what the DMC needs.

Questions submitted during the webinar

Question:
Have you encountered any clinical trials where the DMC recommended discontinuing or stopping the study before the planned interim analysis, based on its review of accumulating safety or efficacy data? If so, what were the key factors behind such recommendations?

Answer:
We can recall two instances. One was cases of renal failure in the experimental group; the other was early deaths in the experimental group. The latter phenomenon became known as “death as a first event”. The need for termination was so obvious in these cases that there was no push back from the sponsor. In another case we asked the sponsor to compute conditional power. They said that this is only done at planned interim analysis and there was no such analysis in this protocol. Eventually they agreed and the trial was stopped. Most clinical trials do not have a planned interim analysis. Yes, either it is clear the important safety signal is not balanced with any change of benefit or there is little help of completing the trial as planned. The latter is very rare without a formal futility analysis.

Questions submitted during the webinar

Question:
Compare and contrast a DMC and internal benefit-risk committee.

Answer:
Some pharma companies have internal DMCs in addition to the external independent DMCs. The internal DMCs usually consist of sponsor MDs and statisticians who work in a different disease area than the one for the internal DMC that they will serve on. The internal group can meet at a moment's notice, whereas getting an external DMC together even for a Zoom session takes time. The internal committee cannot veto an external DMC decision. They do not meet regularly, only when needed for an opinion on something that just happened, like a case of endophthalmitis in an ophthalmology trial. The external DMC is always made aware of questions posed to the internal DMC. We have not experienced any conflicts. This all needs to transparently spelled out in the charter. It also depends on whether it is an open or double-blind trial.

PHUSE Working Groups

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- Data Transparency
- Nonclinical Topics
- Real World Evidence
- Data Visualization & Open Source Technology
- Optimizing the Use of Data Standards
- Risk Based Quality Management
- Emerging Trends & Innovation
- pharmaverse
- Safety Analytics



The door is always open

PHUSE Safety Analytics Working Group

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Current Projects

- Analyses & Displays for Hepatotoxicity
- Best Practices for Informing Benefit-Risk and Communicating Safety Information
- Estimands in Safety Analytics
- Interactive Analyses and Displays for Laboratory Data
- Process for Aggregate Assessment of Clinical Trial AE Data
- Safety Analytics Education

More info

Today's Sponsor

Upcoming PHUSE Webinar

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The Statistician, the Clinician, and the Hot Water Heater

- **Thursday, December 10 at 9-10am ET**
- A conversation with **Janet Wittes** and **Walter Straus** about how statisticians and clinicians need to use mutually understandable language to address complex health problems, drawing lessons from a Legionnaires' disease investigation and careers of successful collaboration

Info and registration

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THANK YOU!