

## **Data Monitoring Committees: Promoting Best Practices**

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- \* Ellenberg SS, Fleming TR, and DeMets DL: “*Data Monitoring Committees: A Practical Approach*”, John Wiley & Sons, 2019, Second Edition
- \* **Fleming TR et al. “Data monitoring committees: Promoting Best Practices To Address Emerging Challenges”. *Clinical Trials* 2017; 14: 115-123**
- \* Fleming TR, Ellenberg SS, DeMets DL: “Data monitoring committees: Current Issues”. *Clinical Trials* 2018; 15: 321-328

# Mission of the DMC

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Uli Burger  
Paul Gallo

- To Safeguard the Interests  
of the Study Participants
- To Preserve Trial Integrity and Credibility  
to enable the clinical trial to provide  
timely and reliable insights  
to the broader clinical community

## Some Fundamental Principles in Achieving the DMC Mission

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To assist the DMC in achieving its Mission,  
procedures are needed...

- To reduce pre-judgment of interim data
  - ⇒ *Maintaining confidentiality of interim data*
- To guide the interpretation of interim data
  - ⇒ Group sequential monitoring boundaries
  - ⇒ Unbiased judgment
    - ... *Well-informed*
    - ... *Independent*

... Motivates fundamental principles  
for DMC functioning and composition...

# Some Fundamental Principles

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- DMC should have *Sole Access* to interim results on relative efficacy & relative safety of interventions
- DMC should have *Multidisciplinary* representation having experience in the DMC process
- DMC should be *Independent* with freedom from apparent significant conflicts of interest ... financial, professional, regulatory

## DMC: Best Practices

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*An Opinion:* The DMC process  
for monitoring randomized clinical trials  
is *not* better than it was 10 years ago !

In particular, ongoing and emerging challenges  
threaten the DMC's *independence* and effectiveness...

Best practices and operating principles  
for effective functioning of DMCs  
have been proposed to address these challenges

## DMC: Best Practices

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- An expert panel of representatives from academia, industry and government sponsors, and regulatory agencies met in June 2015 to discuss ongoing and emerging challenges potentially threatening DMC's independence and effectiveness
- A position paper was published in 2017 in *Clinical Trials* to summarize these discussions and to offer the authors' recommendations to improve the DMC process
- The authors of the *Clinical Trials* article:  
TR Fleming, DL DeMets, MT Roe, **J Wittes**, KA Carim, AN Vora, A Meisel, RP Bain, MA Konstam, MJ Pencina, DJ Gordon, KW Mahaffey, CH Hennekens, JD Neaton, GD Pearson, TLG Andersson, MA Pfeffer, SS Ellenberg

\* Fleming TR et al. "Data monitoring committees: Promoting Best Practices To Address Emerging Challenges". *Clinical Trials* 2017; 14: 115-123

# Proposed Best Practices and Operating Principles

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- Achieving adequate training/experience in DMC process  
*Didactic instruction; Apprenticeship model*
- Indemnification
- Addressing confidentiality issues  
*Linked DMCs: Thomas Jaki*  
*Frontloading: Lisa Squassante*
  - Maintaining confidentiality:  $\downarrow$  pre-judgment  $\Rightarrow$   $\uparrow$  trial integrity
  - DMC needs *ongoing* access to *unblinded* efficacy & safety data
  - Access by others should be limited to a ‘need-to-know’ basis
  - Need for a Mediator, balancing ethical & legal responsibilities  
*Steven Teerenstra*
- Implementing procedures to enhance DMC independence
  - DMC Meeting Format *Closed / Open / Closed Sessions*
  - Creating an Effective DMC Charter:  
*...providing guiding principles, not rigid requirements*
  - DMC recommendations through *consensus*, not by *voting*
- Defining the role of the Independent / Reporting Statistician  
*Janet Wittes*  
“Data monitoring committees: Promoting Best Practices *Clinical Trials* 2017; 14: 115-123

