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MRC Clinical Trials Unit Hub

The potential for central monitoring techniques to replace on-site monitoring in clinical trials: a review of monitoring findings from an international multi-centre trial

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Can central monitoring techniques identify on-site monitoring findings? A review of findings from selected monitoring reports in a phase III trial.

- Aim: to assess the type and proportion of on-site monitoring findings that can be identified through the use of central monitoring techniques.
- Methods: retrospective analysis of on-site monitoring findings
  - Findings extracted and individually assessed to see if they could have been detected in the trial database or through other central means

MDP301 trial

- Setting: Microbicides Development Programme 301 trial.
- Randomised, placebo controlled IMP trial of microbicide gel to prevent vaginally acquired HIV infection, conducted in 6 sites in East and Southern Africa
- 9385 healthy women enrolled, 4 wkly clinic visits for up to 24 months follow up
- Intensive on-site monitoring plan designed to complement trial management processes as results were intended to support licensing application to US FDA had they been positive

MDP301 trial monitoring

- Trained staff visited sites according to pre-specified schedule
- Checking informed consent forms, data management systems, pharmacy accountability
- Source data verification
- Findings: critical, major or other
- Common database in place at each site including double data entry system for validation
- Combined database at CTU
- Query module designed to allow detection of missing data, missing CRFs, defined inconsistencies and to enter query resolutions

Retrospective review process - methods

- Review of
  - On-site monitoring reports
  - PMBe reports
- Individual findings extracted and assessed
- Findings relating to data points
  - In query module?
  - Could a query have been designed and included?
- Findings not relating to data points ie TMF review, trial processes and procedures
  - Could some other central process have been implemented to identify it?

Summary of review findings

Summary of findings	Site monitoring	PMBe report monitoring
Number of participant files reviewed	104	~1100
Number of study visits contributing to review	324	~3500
Number of findings	**268**	**9**
Findings that were critical or major	2 (2 major)	9 (3 critical, 6 major)
Findings identified on the trial database as well as directly during on-site monitoring	76 (28.4%)	-
Findings assessed as possible to have been identified using other central monitoring strategies	179 (66.8%) (2 major)	7 (3 critical, 4 major)
Findings assessed as unlikely to have been identified without a direct review of the participant folder or through other central monitoring process	13 (4.9%)	2 (2 major)

Composite central strategy to identify finding

Central strategy	N (%) of total monitoring findings
Specific data check could have been written	70 (39.1%)
Use of centralised or electronic data capture procedures	38 (21.2%)
Central receipt & review of ppt info (inc translations)	22 (12.3%)
Central receipt & review of spec testing logs	17 (9.5%)
Central receipt & review of screening/enrolment logs, IC forms, delegation of responsibility logs	12 (6.7%)
Central receipt & review of reg docs	6 (3.4%)
Central receipt & review of source data on NAEs	2 (1.1%)
Central receipt & review of pharmacy accountability docs	1 (0.6%)
Central receipt & review of translated CRFs	1 (0.6%)
Fax back confirmation of docs filed	6 (3.4%)
Review of delay between date of visit and date data entered onto CRF	2 (1.1%)
Including all written text/comments on database	2 (1.1%)
Total	179

Central strategy considerations and the use of data checking

- Who decides what to check and how?

- Does everything need checking?
- Size of trial – number of sites, participants, volume of data/information, site visit schedule
- Type of trial – level of risk to participants

- Queries can be written for any linked data in a trial

- Financial burden
  - Programming – writing and testing
  - Central management - running and chasing
  - Site management – responding

Conclusions

- Central monitoring – trial related QC activities
- On-site visits/monitoring – where central review or RA indicates increased cause for concern

- Benefits of on-site meetings
  - Staff motivation
  - Scientific & clinical trial capacity development
  - Communication with remote sites
  - Staff training

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