Pre-meeting input to DSBS Gå-hjem-møde: Statistical Oversight, 22-oktober-2025

Themes for the group discussion are provided on page 2 to 6.

Please note: references, sub questions and comments may not be complete nor cover all aspects.

Schedule may be adapted.

Themes

Theme	References to ICH E6(R3)	Sub questions (for inspiration)	Comments/examples
1. Qualification process	3.6.6-3.6.8	What is the role of biostatistician during the Request for Information (RfI) and Request for Proposal (RfP) process? Challenges in identifying the 'appropriate' service provider? What detail level of sponsor audit is sufficient? What to request for information in order to identify potential challenges etc? How to review budget? Consider complexity of analysis programs needed	E.g. sponsor access to Service Providers Quality System (guideline does not specify scope, timing and duration – is that an issue?) Apparent disconnect - between CV and actual work experience for Subject Matter Expert (SME). SME-SMEsessions may be valuable Pay attention to data transfer and SDTM/ADaM/TFL count (typically underestimated), and number of review rounds/dry-runs Does this with counting basic TFLs even make sense anymore? Service providers most likely have a standard macros library Organization chart should be shared (applicable part only)
2. Statistical oversight during trial conduct	3.6.9, 3.9, 3.11.4.5.4	What is a sufficient level? Is it the same for all trials/projects? Risk-proportionate approach; where and how do you/your company implement this? Where has it worked and where can we be better?	An idea is to have one person to screen and send back immediately to save other Subject Matter Experts (SME's) time and for it NOT to count as a review round Screening of document: header, footer, pagination, dates correct, no missing cross

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		How is the process around quality tolerance limits (QTLs, ICH E6 R2) definitions in your company?The ICH E6 R3 term is "acceptable ranges". How are they defined and monitored? Who owns them? How to prioritize what to review? What and how do you document oversight? Review process and timelines. Definition of review and approval of documents. Change control and version control. For example: how many drafts before final, schedule for review, what does a Sponsor review imply – good to include as part of responsibility split. What does the statistician in your company approve? And what does "Approval" imply?	references, references correct, names correct, reference to other documents correct (especially attention to version) A challenge is that often we do not have oversight with service provider's internal review – should be documented in electronic Trial Master File (eTMF) Important that the service provider incorporates sponsor comments into their timelines
3. Statistical programming and data analysis	3.16.2	Data checks – who does what? What are we as statisticians responsible for checking? Triple programming – when is it necessary? How much can be shared from a previous trial to have similar reporting structure etc.? Budget deduction? Sponsor access to analysis programs in the analysis phase – has this been a challenge for you/your company?	Traceability and clear communication of data handling decisions is a common challenge When is CDISC deliverables made available for Sponsors review – during or after TFL production? Confirmatory endpoints, selected secondary endpoints, complex endpoints, important safety, other? Audit trail requirement

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		What about proprietary standard macros from the SP – often reluctant to send when a study has been finalized – what is the experience? Options for procedures – how to specify and where?	Could be a need to actually understand what the SP has done wrt. analysis Important for regulators to be able to understand and reproduce results. E.g. skeleton for visit structure for an MMRM?
4. Documentation of oversight	3.6.6, 3.6.8, 3.6.9, 3.9, C.1.3, C.3 (see also Essential records table)	How to document your oversight for specific tasks – how is it done in your company? How best to ensure the Trial Master File (TMF) is inspection-ready for the documents we are responsible for? Is it necessary to document review of dry-runs?	Oversight should be part of the TMF – could a common oversight log be a way forward? Who, what, when etc.
5. Quality	3.10, 3.11, B.12	Should there be trust until proven otherwise? And what could be good strategies for catching elements not up to the required/expected quality? When to escalate if quality expectations is not met? And how to mitigate?	As a SME, it can be difficult to be the one who have to tell your close collaborators when things are not good enough

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6. Collaboration between sponsor and service provider	II.10	How best to ensure good collaboration between the two (or more) parties? How best to ensure proper knowledge transfer from sponsor to service provider? How best to ensure alignment of expectations to deliverables?	One or more SME-SME kick-off meetings prior to initiation of specific tasks (e.g. SAP authoring) has shown to be somewhat efficacious
7. Technology and methodological advances	II. 2.3	What is feasible within the next, say, 3 years? Realistic? Relevant? Technology - Devices - Digital Health - Other Data sources - Collaborative editing - TLFs from first randomized patients - CSR generation automated from TLFs and other applicable documents - AI based data validation - AI generation of study documents (including SAP) - Automated generation of minutes - Issue management tools (combining several aspects, such as EDC data review, query status, validation checks, P21 report findings, TLFs review findings, source code review findings, double programming findings) Methodological advances - Statistical methods: estimands, individual subject predictions - Digital twins (ProCova, historical data, etc)	How much experience does Sponsor need before emarking on “new” technology respectively methods? Same question also for Service Provider?

Schedule

Schedule

Time	Description
>14:30	Arrival
15:00	Welcome, presenter: Randi Grøn, DSBS chair
15:05	Introduction – group discussion, themes, E6(R3) comments Presenter: Marc Andersen
15:20	Group discussion in pre-assigned groups. Each group selects 3 themes to discuss after Break 1
15:35	Break 1
15:45	Group discussion in the assigned groups – suggest using 20 min for each theme. Pre-assigned: • facilitator – to guide discussion if needed • notetaker – one of the organisers
16:45	Break 2 – notetakers meet and create draft summary as start for a draft report
17:15	Notetakers present summary. Open discussion, all
17:25	Close out, how to proceed. Presenter: organisers
17:30	Thanks for today!

Group discussion

Group discussion

- Consider discussion from different perspectives, e.g. Sponsor and Service provider
- For real life examples suggest to anonymize company names and regulatory bodies
- Do not be shy in presenting opposing views / approaches
- Provide concise summary for the notetaker
- The notetakers will present draft summary of the group discussion after Break 2
- Next step: draft summary to be distributed among meeting participants. Then decide next step.

Online discussion – see teams invite for link