Table 6: Phase Dependent Requirements for Method Validation Across the Globe

SESSION 1:
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SESSION 2:
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SCOPE:
Validation of analytical procedures during clinical development is an evolving process. According to EMA (EMA/CHMP/BWP/534898/2008 rev. 1, 14 Sep. 2017), for phase I and II clinical trials, the suitability of the analytical methods used should be confirmed. Parameters should be chosen as appropriate. For phase III, analytical methods used for release and stability testing should be validated, by the end of phase III full method validation must be completed, including confirmation of robustness.

QUESTIONS FOR DISCUSSION:
1. What are the expectations of Health Authorities? How to interpret their guidelines? Different requirements for EU and US.
2. What is phase-appropriate? Which parameters should be validated for which clinical phase?
3. Can (non-GMP) data from research be leveraged for early phase? Can method monitoring data replace parts of late-phase validation?
4. Is multi-product validation sufficient for generic methods (e.g. UV, SEC)? How to show product-specific suitability?

DISCUSSION NOTES:

Topic	Discussion at Round Table
What are the expectations of Health Authorities? How to interpret their guidelines? Different requirements for EU and US.	• There are different requirements with regards to data expected from method validation in different phases (e.g. EU vs US) → guideline differ slightly • Typically companies would follow the more restrictive guideline since data will most likely be submitted in EU, US and several other countries • Validation Plans and/or Results (if available) are submitted at Phase 1
What is phase-appropriate? Which parameters should be validated for which clinical phase?	• Ph1 and Ph2 rather done qualification (specificity, reproducibility and linearity), validation before Ph3 is kind of a re-evaluation of method • full validation for PPQ (at latest) including robustness, accuracy, LoQ/LoD • In order to avoid problems in later stages, tendency to create (too) many data early on. Depends on molecule and method performance

Can (non-GMP) data from research be leveraged for early phase?	• Might be possible depending on method: - e.g. Linearity should be performed by QC labs with the protocol established for GMP production - e.g. robustness could also be in non-GMP environment • Non-GMP data is leveraged for method assessment, however not validation (i.e. PPQ) • "Reliable" data sourcing of method validation data is important, already in research environment (validation plan not necessarily available in research ??) → consider setting up a holistic validation strategy by evaluating the following aspects for each method: o in which environment (GMP, non-GMP) should validation be performed o whether it is OK to leverage validation data from research o how the method is controlled during actual testing (daily/weekly method monitoring, system suitability test) o current phase: development phase or Marketing application
Can method monitoring data replace parts of late-phase validation?	• Trending data are leveraged for method understanding, but not yet for method validation • Yes, this may be a good idea → data from method monitoring (trend charts/ analytical report) can be leveraged for Ph3 validation but also for method development – may even replace precision experiments? Monitoring is done over larger timeframe, validation only within some weeks. • Example method monitoring: % CPA (main peak, acidic/basic regions), retention time, mobile phases (expiration time, lot No. but also analyst, failed runs)
Is multi-product validation sufficient for generic methods (e.g. UV, SEC)? How to show product-specific suitabiliy?	• Might be OK if same method/instrument is used for standard antibodies • Should be allowed for "robust" methods. Problem: how to define what is "robust" • However, there is also experience that even one out of many standard antibodies behaved different → therefore might be critical • Clear scientific rationale required to defend this strategy but it´s an interesting thought
Automatic validation software e.g. CAYMAN used?	• validated software can (should?) be used whenever possible. Statistics in phase 1 often not as sophisticated as statistics in Ph3