Roundtable Session – Table 5 - GMP Inspection Roundtable – Key Takeaways for Regulatory Affairs CMC

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Abstract:

Good Manufacturing Practice (GMP) and Chemistry, Manufacturing and Controls (CMC) are closely connected, but they sit within distinct regulatory responsibilities. Assessors evaluating the CMC part of a marketing authorisation application focus on the quality data submitted to support the manufacturing process, control strategy, specifications, stability, and overall assurance of quality. GMP compliance assessment remains within the remit of GMP inspectors and the relevant inspection processes.

This round table aims to provide an open forum to discuss the points of interaction between CMC assessment and GMP-related considerations, without shifting the discussion into formal GMP compliance evaluation. The intention is to explore how CMC assessors can appropriately consider information that is linked to manufacturing practice, site readiness, process and analytical method validation, technology transfer, data reliability, and lifecycle management. The discussion will focus on practical experiences, areas of interface, and opportunities for clearer communication between CMC assessors, GMP inspectors, and applicants.

Proposed questions:

1. Where do GMP inspection-related aspects most often intersect with the CMC assessment of a marketing authorisation application, and where would greater clarity be helpful?

2. What lessons has industry learned from cases where CMC assessment and GMP inspection processes interacted particularly well — or less well?

3. Where do applicants perceive overlap, gaps, or uncertainty between questions raised during CMC assessment and topics addressed during GMP inspection?

1. Growing overlap between GMP inspections and CMC review

- The boundary between GMP compliance and CMC dossier content is becoming increasingly blurred.

- A recurring example is the **control strategy during devlp**: regulators often expect scientific justification for parameters and acceptance criteria, while industry may view much of this information as GMP-managed knowledge rather than filing content.
- This creates tension around how much supporting data should be included in the dossier versus retained within the Pharmaceutical Quality System.

2. Data integrity expectations extend beyond traditional GMP records

- Discussion centered on whether development and characterization data should be held to GMP-level data integrity standards.
- While characterization studies are generally **not expected to be conducted under GMP**, they must be scientifically robust, traceable, and reliable.
- Reviewers may become concerned when inconsistencies exist between characterization data, process understanding, and batch analysis results, potentially triggering broader questions about data integrity and product understanding.

3. Transition from development to QC remains challenging

- Questions arose regarding how data generated in development environments should be transitioned into GMP/QC operations.
- The group acknowledged that while early development work may not be GMP-compliant, the underlying scientific rationale supporting the control strategy must remain credible and defensible throughout the product lifecycle.

4. Emerging analytical technologies create inspection challenges

- New methodologies such as advanced mass spectrometry may be introduced in Phase 1 or Phase 2 using software platforms that are still evolving.
- Although the analytical science may be mature, supporting software may not yet have fully validated audit trails or complete computerized system controls.
- Such issues are generally viewed as **GMP inspection topics rather than CMC review concerns**, provided the science remains fit for purpose during early development.

5. Prior knowledge and lifecycle use of analytical data

- There was discussion around leveraging prior knowledge generated using non-GMP methods.
- Participants generally agreed that scientifically sound prior knowledge can support platform understanding regardless of whether it originated under GMP conditions.
- However, current expectations typically require method qualification or verification activities to be repeated when methods are transferred into GMP environments or new manufacturing/testing sites, particularly for late-stage development and commercialization.

6. Pre-Approval Inspection (PAI) considerations

- Questions were raised regarding circumstances under which regulators may rely on inspection outcomes from other authorities.
- Reliance may be influenced by factors such as Mutual Recognition Agreements (MRAs), inspection history, and whether inspections were conducted by recognized partner authorities.
- Inspections from third-country regulators may not always satisfy EMA or other health authority requirements.

7. Inspection-related document requests during review

- In some cases, reviewers may request GMP-related documentation during dossier assessment.
- Examples discussed included requests for inspection information or quality management records when questions arise regarding manufacturing controls.

8. Product Quality Review (PQR) as evidence of control strategy effectiveness

- A strong Product Quality Review was viewed as an important demonstration that the control strategy is functioning as intended.
- PQRs provide inspectors with evidence that process performance, product quality trends, deviations, and CAPAs are being actively monitored and managed within the Pharmaceutical Quality System.

Overall Theme

The discussion highlighted that regulators increasingly expect a **seamless connection between product knowledge, control strategy, data integrity, and GMP execution**. While development and characterization activities may not require full GMP compliance,

the scientific data underpinning regulatory submissions must remain reliable, traceable, and consistent, as deficiencies can quickly become both a review and inspection concern.

GMP Inspections Roundtable – Key Takeaways

The discussion focused on the increasingly blurred boundaries between GMP compliance and CMC regulatory expectations, particularly regarding control strategy justification and the extent of supporting data that should be included in regulatory submissions versus maintained within the Pharmaceutical Quality System.

Participants emphasized that while development and characterization activities are not generally expected to be conducted under GMP, the underlying data must be scientifically sound, traceable, and consistent, as discrepancies can raise reviewer concerns and trigger broader data integrity questions.

Emerging analytical technologies and evolving software platforms present additional challenges, with data governance and system validation typically falling within GMP inspection scope rather than CMC review. The group also discussed the use of non-GMP prior knowledge, noting that while such data can support product understanding, qualification and verification activities are generally expected when methods are transferred into GMP environments.

Additional topics included regulatory reliance on inspection outcomes from other authorities, circumstances under which GMP-related documentation may be requested during dossier review, and the importance of Product Quality Reviews (PQRs) as evidence that the control strategy is effectively maintained throughout the product lifecycle.

Overall Theme

The discussion highlighted that regulators increasingly expect a **seamless connection between product knowledge, control strategy, data integrity, and GMP execution**. While development and characterization activities may not require full GMP compliance, the scientific data underpinning regulatory submissions must remain reliable, traceable, and consistent, as deficiencies can quickly become both a review and inspection concern.

Final verbal output

The discussion underscored a fundamental shift in regulatory thinking: regulators increasingly view product development, CMC review, and GMP compliance as a continuum

rather than separate disciplines, creating new expectations for how scientific knowledge, data integrity, and control strategies are generated, justified, and maintained throughout the product lifecycle.

Key Discussion Points:

- The boundary between GMP requirements and CMC dossier content is becoming increasingly blurred, particularly regarding the level of scientific justification expected for control strategies and critical process parameters.
- While development and characterization studies are not generally expected to be conducted under GMP, the underlying data must be scientifically robust, traceable, and internally consistent, as discrepancies can raise both review and inspection concerns.
- Emerging analytical technologies and evolving software platforms present challenges where scientific capability may outpace GMP system maturity, placing increased focus on data governance and computerized system controls during inspections.
- Participants discussed the use of non-GMP prior knowledge and development data, noting that such information can support product understanding, although qualification and verification expectations typically increase when methods are transferred into GMP environments.
- Additional discussion topics included reliance on inspection outcomes from other regulatory authorities, circumstances under which GMP-related documentation may be requested during dossier review, and the role of Product Quality Reviews (PQRs) in demonstrating the ongoing effectiveness of the control strategy.

Overall Takeaway:
Regulators and industry broadly aligned on the expectation that the scientific evidence supporting a product's control strategy must remain reliable, traceable, and defensible across development, regulatory review, and GMP inspection, as weaknesses in one area increasingly have implications across all three.