Quality by design (QbD) is a global regulatory initiative with the goal of enhancing pharmaceutical development through the proactive design of pharmaceutical manufacturing process and controls to consistently deliver the intended performance of the product. The principles of pharmaceutical development relevant to QbD are described in the ICH guidance documents (ICHQ8-11). QbD encourages implementation of risk-based approaches that allow both industry and agency to focus attention on critical areas. In addition, the enhanced process and product understanding can offer advantages over the traditional approach, including a more focused control strategy and incorporation of additional flexibility into the process.

QUESTIONS FOR DISCUSSION:

1. Have QbD concepts been embraced by your company?

2. To what extent are you implementing QbD concepts? Are QbD-like concepts part of your strategy for CQA identification, control strategy decisions, process/CPP/design space decisions, and/or lifecycle management decisions?

3. What has been your experience with global regulators on specific QbD approaches?

4. What are the current challenges?

5. Is the value of QbD being realized?

NOTES:

- Discussion on "Enhanced Understanding" versus "Enhanced Process Design" versus "QbD". Some disagreement on whether these terms are the same or different; however, general agreement that a design space is not a requirement
- Clear differentiation between systematic enhanced development versus design space, especially from a regulatory filing and flexibility perspective
  - Design space can be a potential outcome of enhanced process design
- Has there been success in reducing regulatory burden via enhanced process design?
  - Other than increased knowledge or a process and product, group agreed there was no clear regulatory flexibility benefit even with design space especially with amount of work put into true design space in BLA
- Overall agreement that increased knowledge has more potential for increased flexibility (eg. tech transfers or other changes)
- Group agreement that regulatory flexibility benefits both industry and regulators
- Discussion on the QbD EMA/FDA pilot program overview: Industry/agency views on design space: What constitutes what is in the design space?
- There are industry and agency disagreements on methodology for determining "criticality," which heavily depends on the definition of criticality within the companies individual quality system
  - For non-critical attributes, evaluation of residual risk is still required. There was a perception that Health Authorities still have a general discomfort with attributes near the cutoff, as the cutoff may be arbitrary. It was noted that there
needs to be a cutoff and associated risk assessment, and a perception that Health Authorities are being too conservative.

- Always uncertainty and can never eliminate, but is in line with ICH guidance on risk-based approaches
- Group recommends to approach agencies and gaining agreement on companies' methodology for enhanced process and product understanding
- Non-CPPs: Recommendation from the group to continue to study and build on historical data and understanding

- Enhanced versus PAT:
  - Group agreement that PAT can be a result of enhanced process and product understanding, but can be difficult for smaller companies due to cost, time required, and capability. It was noted that this can also be challenging if working with a CMO.

- How have QbD concepts been implemented at larger vs small companies and what is agency perception?
  - Same scrutiny for all but potential different view on the types of molecules (e.g. small vs. biologics)

- Global regulatory environment:
  - QbD design space complexity and benefit is questionable in the global environment
  - There are definitely benefits of Enhanced Understanding for both industry and regulators; benefit is variable both within agencies and across different Health Authorities