Table 37: Challenges in Meeting Global Pharmacopoeia Requirements – Strategies to Harmonize

Facilitators –

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Scope:

Compliance with requirements published by pharmacopoeias around the world is a legal and regulatory requirement for companies operating globally. The test methods, monographs and general chapters published by pharmacopoeias affect the entire lifecycle of a product. During development and late-phase clinical trials each company must establish an appropriate standard of quality to ensure that drug substance and drug product consistently meet the defined quality profile. The compendial compliance is required when a drug is submitted to regulatory agencies to gain marketing approval. There is merit to ensure compendial compliance already during the development stage, to ensure a smooth product launch and commercialization.

Challenges arise, when regulatory expectations and processes differ between different regions, e.g. with regards to acceptance criteria or analytical approaches used to evaluate the material and/or product. Once a drug product is licensed, the manufacturer must comply with their approved registration and with applicable monographs and associated general chapters, along with other applicable content in the pharmacopoeias.

Many pharmacopoeias support initiatives for harmonization, to establish consistent, global pharmacopoeia standards. This roundtable session will provide opportunity for participants to discuss challenges, share perspectives and successful experience on how to meet health authority expectations to comply with pharmacopoeia requirements, and deliver quality medicines that extend and improve the lives of patients worldwide.

Questions for Discussion:

No questions included at this time.

Discussion Notes:

January 26 and 28, February 1 and 4, *combined* –

~40 global pharmacopoeias – how do we manage?

- How do we manage variations in methods such as pH and osmolality?
    - Example 1: internal test method that attempts to include elements of major pharmacopoeia
        - do not claim specific pharmacopoeial references in writing but do communicate (eg., in response to questions) that procedure is aligned with pharmacopoeia
        - verify, do not validate
    - Example 2: internal test method that includes elements from major pharmacopoeia
        - claim compliance to applicable pharmacopoeia
        - within QMS we document justification of any variation
    - Example 3: internal test method that operates according to all major pharmacopoeia
        - example: pH temp setpoint of 23C to accommodate all 3 pharmacopoeia
        - have had success claiming JP chapter in US BLA
- how do companies manage chapters that come with generic criteria, such as subvisible particles USP <787>/<788> with NMT 600/6000 particles per container?
    - some have gotten requests from agencies to set product-specific specifications
    - these chapters specifically allow microscopic analysis as an alternative (this was acceptable to regulator in this example)
- how do companies manage the difference in the USP/JP/EP acceptance criteria for visible particles (essentially free/practically free from visible particles vs free from foreign insoluble matters)?
    - focus is on extrinsic particles
    - intrinsic particles may be justifiable in protein products
    - technically there must be a certain acceptability of intrinsic particles
    - can use a statistical approach based on batch size (AQL) to determine number to test - > if 100% pass, call “practically free” of visible particles
        - some companies test on a single vial
    - on stability – how to test?
        - test 1 vial
        - after AQL release, test 1 – if no pass then test 3 and require 100% pass
        - pull multiple vials (and consider putting back? how would you track this?)
    - what if volume is too small?
        - consider combining – but have to control not to introduce particles
- how do we verify and document the suitability of pharmacopoeial methods?

    - for simple methods, compare to expected range for confirmation
    - document verification at all testing labs
- what are options for driving harmonization among regulators and pharmacopoeias?
    - Could this be a good topic for IQ Consortium?