EMA/ FDA Workshop on
support to quality development in early access **approaches**

Perspective on GMP Considerations for Accelerated Access

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Outline

- Overview of principles
- Case Study
- Perspective on key challenges
- Summary and Recommendations

- Backups: other topics for consideration

Introduction: Global view of GMP

Foundational Principles

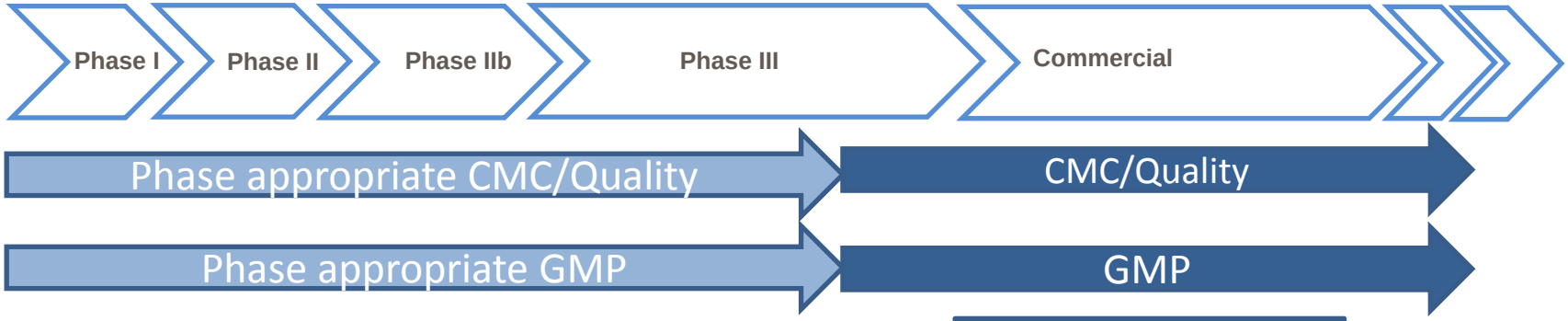
- GMPs are essential to ensure quality and protect patients, and many elements are common to the clinical and commercial phase
- GMPs globally are well harmonised (cf PIC/S, MRAs, etc)

Considerations for accelerated scenarios

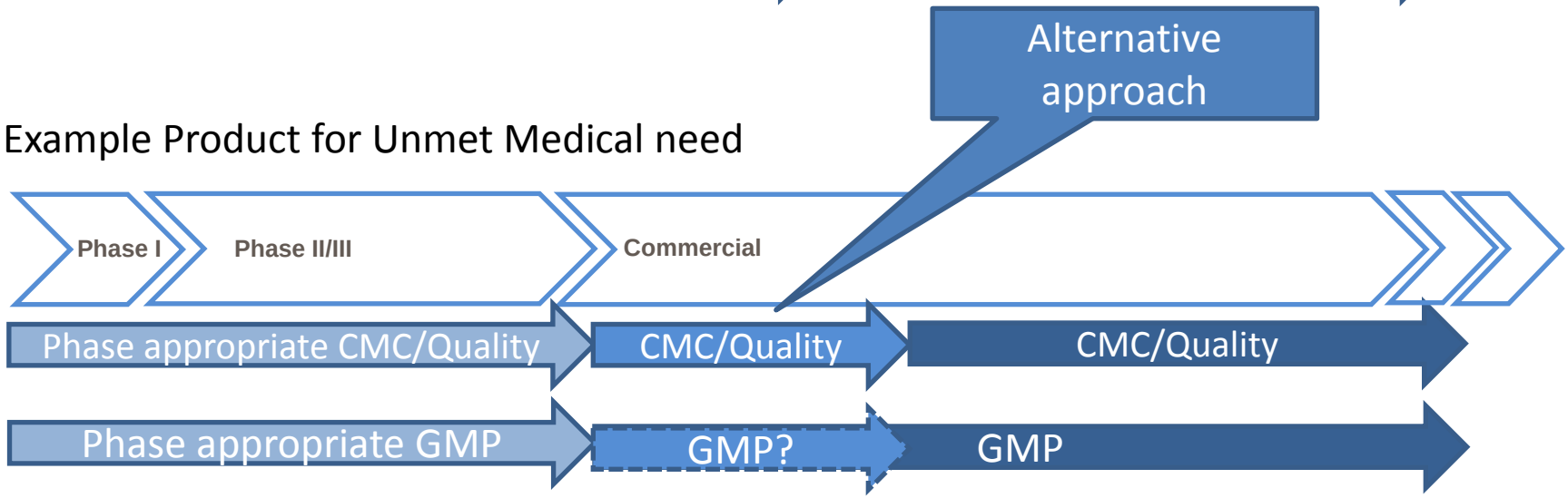
- Continuity of supply is an essential consideration for critically ill patients (e.g. for continued supply to cancer patients)
- Initial commercial supply may be for small numbers of patients & unmet medical need
- The pace of development may mean that supply chains require the use of supply chains typically associated with clinical supply (IMPs)
- GMP considerations for the clinical phase may be appropriate for early commercial supply

Accelerated Access Development and Manufacture

Traditional Development



Example Product for Unmet Medical need



Are there different GMP considerations where **manufacturing sites only supply limited numbers of products to small numbers of critically ill patients for a limited period of time?**

EFPIA Example Scenario

- Cancer product where early clinical data shows efficacy
- Phases 2 and 3 are a single study supplied from IMP (clinical) site
- Need for rapid file and launch ensuring **continuity of supply to patients**
- Introduction of commercial manufacturing site (<10-fold increase in scale, similar manufacturing process) on critical path – slower file and launch.
- Sponsor believes commercial supply cannot be supported from IMP site, with no commercial GMP licence

- More rapid commercialisation if the sponsor **uses IMP sites for early commercial supply**
  - IMP sites are ideally suited to rapid scale up and manufacture.
  - Skilled at rapid introduction of new products
  - Scale-up and experience is a key part of building process knowledge.
  - Systems and processes adapted to sceanrios where knowledge is more limited and unforeseen events and deviations will occur more frequently.

GMP considerations

- GMP considerations for the clinical phase can be appropriate for early commercial supply for unmet medical need
- Example areas of difference
  - Labelling - tamper evident device and unique identifier.
  - Cleaning verification approach
  - No Validation/PPQ for processes and methods
  - Expectations for data trending and lifecycle analysis
- Foundational elements of GMP are common to clinical and commercial supply

- **Greater clarity on clinical phase GMP considerations could be helpful to support early commercial supply for unmet medical need**

Commercial Supply from IMP Sites

- Early commercial supplies may need to come from sponsor's IMP sites or CROs targeted at IMPs.
- This can bring significant GMP challenges – augmented by a lack of clarity on phase appropriate GMP and inspectional outcomes
- Product can be demonstrated to be equivalent to the commercial product
- Product Licenses differ across regions and even EU member states, for example:
  - UK requires general IMP and product specific commercial supply licenses
  - Italy requires separate licence for each IMP
  - US no IMP license

Can an applicant supply commercial product from an IMP site without a licence?

Dialogue with regulators

- Dialogue and problem solving through scientific advice/type C meetings are a key element of PRIME/BTD
- Are there robust mechanisms to ensure GMP considerations can be discussed (e.g. with inspectors in OPQ, or IWG members in EMA)?
- Example topics to agree:
  - Site licence requirements
  - Site manufacturing readiness plan and PACM protocols
  - Labelling considerations
  - Process validation (PPQ) approach
  - API starting materials –designation of different (late stage) starting materials for early commercial supply

How can we ensure alignment between outcomes at scientific meetings and GMP inspections from national competent authorities?

Overall Culture of Review versus Inspections

- Potential disconnect between approach to accelerated **file quality/CMC review and approval** versus **GMP inspection expectations?**
- How do we ensure **both** the review and inspections are aligned?
  - Currently there maybe differences in the expectations from inspectorates even among the major authorities.
  - With the MRA between US FDA and EMA this may address or reinforce such concerns.

How to get the global acceptance of an aligned path forward in this area – how to ensure certainty of inspectional outcomes?

Summary and Discussion Points

- GMP considerations for accelerated access should reflect similar considerations of patient risk/needs as Quality/CMC elements and **focus on the patient and continuity of supply**
- In **accelerated access scenarios**, industry requests regulators to consider:
  - Increased clarity on how GMP considerations for the clinical phase can be appropriate for early commercial supply;
  - Harmonised risk considerations and convergence on GMP inspections, aligned across regions;
  - How IMP sites can be used for early commercial supply without requiring commercial GMP licenses;
  - How PRIME/BT scientific advice procedures be strengthened to allow agreement on GMP matters;

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Back-Ups


Bio
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Other topics

- **Tools for post approval changes** (e.g PACMP protocols) – how can these be utilised as part of a GMP site readiness plan (see Yoko Momonoi talk)?
- **QP discretion** – how can the role and accountability of the QP be utilised to support accelerated access (e.g. consideration of appropriate GMP)?
- **Validation**-opportunities for flexible validation/better use of concurrent validation; considerations for use of non validated API (see Stuart Finnie talk)?