The Role of the Qualified Person

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Agenda

- Licensing
- The Qualified Person (QP)
- Preparation for filing a Marketing Authorisation Application (MAA)
  - Part 1: QP Declaration
  - Part 2: EU Import Testing
- Preparation for Product Launch
- MA Approval and Certification of Launch Batches
- Routine Commercial Supply - Quality Considerations & Challenges

Licensing

Marketing Authorisation (MA)

- A marketing authorisation lays down the terms under which a medicinal product is authorised to be marketed in the EU

Site License (Manufacturers' Authorisation)

- EU pharmaceutical companies hold a Manufacturers' Importers Authorisation (MIA), which is essentially a "site license"
- MIA details the manufacturing and packaging activities that a company is authorised to carry out, and also lists the personnel that are authorized to act as a Qualified Person at the site

The Qualified Person (QP)

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Requirement for the QP

- Legal requirement grounded in EU directives
  (Articles 40-53 of 2001/83/EC)
- Technical, ethical and professional obligations in terms of assuring quality, safety and efficacy of a batch of medicinal product
- Confirmation of compliance with the Marketing Authorisation, EU GMP and the Quality Agreement
- QP bound under a code of conduct and may be held legally responsible by the Member States
- Point of contact for MHRA (or EMA) in case of product investigations

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How to become a QP

- Complete a university degree course in a “defined” scientific discipline
- Minimum of 2 years experience working under an MIA
- Complete a course of study with defined core modules, which are relevant to the pharmaceutical industry
- Undertake an assessment by the representatives of the three professional bodies
- If successful – application and acceptance on the site licence by MHRA

ROYAL SOCIETY OF CHEMISTRY

SOCIETY OF Biology

ROYAL PHARMACEUTICAL SOCIETY

Responsibilities – MAH/QP

- The ultimate responsibility for the performance of a medicinal product over its lifetime, its safety, quality and efficacy lies with the Marketing Authorisation Holder.

- The Qualified Person is responsible for ensuring that each individual batch has been manufactured and checked in accordance with the requirements of the Marketing Authorisation and with Good Manufacturing Practice

Responsibilities - QP

Eudralex Volume 4, Annex 16 ‘Certification by a Qualified Person and Batch Release’ details that the Qualified Person (QP) must

- Personally ensure that the following operational responsibilities are fulfilled prior to certification of a batch for release to market or for export:
  - Certification is permitted under the terms of the MIA
  - Any additional duties and requirements of national legislation are complied with
  - Certification is recorded in a register or equivalent document

Responsibilities - QP

Ensure that each batch is in full compliance with the MA, QTA and GMP/GDP, including steps carried out external to Almac Pharma Services including,

- API manufacture and release; storage and transportation
- Drug Product manufacture, storage and transportation
- Analytical Testing

Preparation for filing an MAA

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Preparation for filing an MAA – Part 1

- Marketing Authorisations must use only Active Pharmaceutical Ingredients (APIs), which have been manufactured in compliance with EU GMP

- Compliance with this requirement is confirmed by a “QP Declaration”, which is submitted with the MAA

- The QP Declaration is issued by a QP at the site with responsibility for Batch Certification as defined in the MAA

- The basis for the declaration will be examined during EU GMP inspections at the releasing sites

QP Declaration for APIs

- Template QP declaration has been issued by the European Medicines Agency (EMA)

- Recommend early discussion to consider and agree the strategy and perform any required audits

- There are specific requirements around the use of third party audits to support the QP declaration

QP Declaration for APIs

Number of prerequisites for a QP Declaration:

1. Quality agreement in place detailing responsibilities

2. Establish the complete supply chain for the API

3. All sites involved in manufacture of the API listed by name, address & function

4. Audits of sites involved in API manufacture have been completed within the last 3 years. Summary details of audits need to be included in the declaration

QP Declaration for APIs

- Of critical importance is the identification of the stage in the API supply chain where “Active Substance Starting Materials” are entered into the process – it is from this point that the QP declaration is expected to cover

- Guidance in Eudralex Volume 4 Part II (excerpt below)

Table 1: Application of this Guide to API Manufacturing

Type of Manufacturing	Application of this Guide to steps (shown in grey) used in this type of manufacturing				
Chemical Manufacturing	Production of the API Starting Material	Introduction of the API Starting Material into process	Production of Intermediate(s)	Isolation and purification	Physical processing, and packaging

Increasing GMP requirements

Preparation for filing an MAA – Part 2

- Identification of the site of import into the EU
- Completion of the release tests listed in the MA following receipt of product in the EU
  - unless product is manufactured/tested in a country with a Mutual Recognition Agreement (MRA) with the EU
- Each batch must be sampled and tested within the EU unless it can be technically justified and documented
  - e.g. sampling of an aseptic product during manufacture
  - any samples taken outside the EU must accompany the batch during shipment

EU Import Testing

- Requires implementation of all release test methods at EU-based analytical laboratories (physical, chemical and biological)
- Initiate with method familiarisation (theoretical and practical)
- Formal method transfer and/or validation (chemistry/ microbiological)
- Formally establish drug product specifications and release test methods in the Almac Quality Management System
  - Or oversight of DP contract labs listed in MAA
- Needs to be formally documented

Preparation for Product Launch

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Preparation for Product Launch

- Need to compile the information which will be relevant to Batch Certification by QP
- Typically based on a “final draft MAA” and confirmed/finalised when approved
- Supply Chain ‘Map’ of active Substance and Medicinal Product up to the point of certification
- Almac Compliance Dossier prepared using the relevant sections of the MAA
- MMA + manufacturing records used by Almac to compile product-specific review checklists
- Full Commercial QTA in place between MA holder and Almac
    - And any subcontracted parties e.g. Contract Laboratory
- QP-QP Agreements between EU drug product sites (if relevant)

Preparation for Product Launch

- Continued communication channels between MA Holder & Almac
- Commercial Manufacture and Package ‘at risk’ pending approval?
- Complete method transfer of drug product release test methods
- Complete audits of drug product sites of manufacture and packaging
- Risk assess and qualify shipping route for product from manufacturing site of production to EU site of importation/packaging and release

Preparation for Product Launch

- Establish mechanisms for:

- Ensuring Almac QP has access to the MA and any variations – management of changes

- Dealing with routine product quality issues

- Routine sharing of manufacturing records

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Commercial Considerations

- Multiplicity of packaging formats required for EU markets

  i.e. leaflet, label & carton

- Development of artworks for EU countries

  eg. blue box labelling, CIP coding

- Implementation of anti-counterfeiting measures

- Identification of distribution sites/partners within EU

- Activities like late stage customisation/blue box labelling – require to be certified by a QP named on MA

- Complexity of supply chain throughout the EU

- Product pricing within the EU

MA Approval and Certification of Launch Batches

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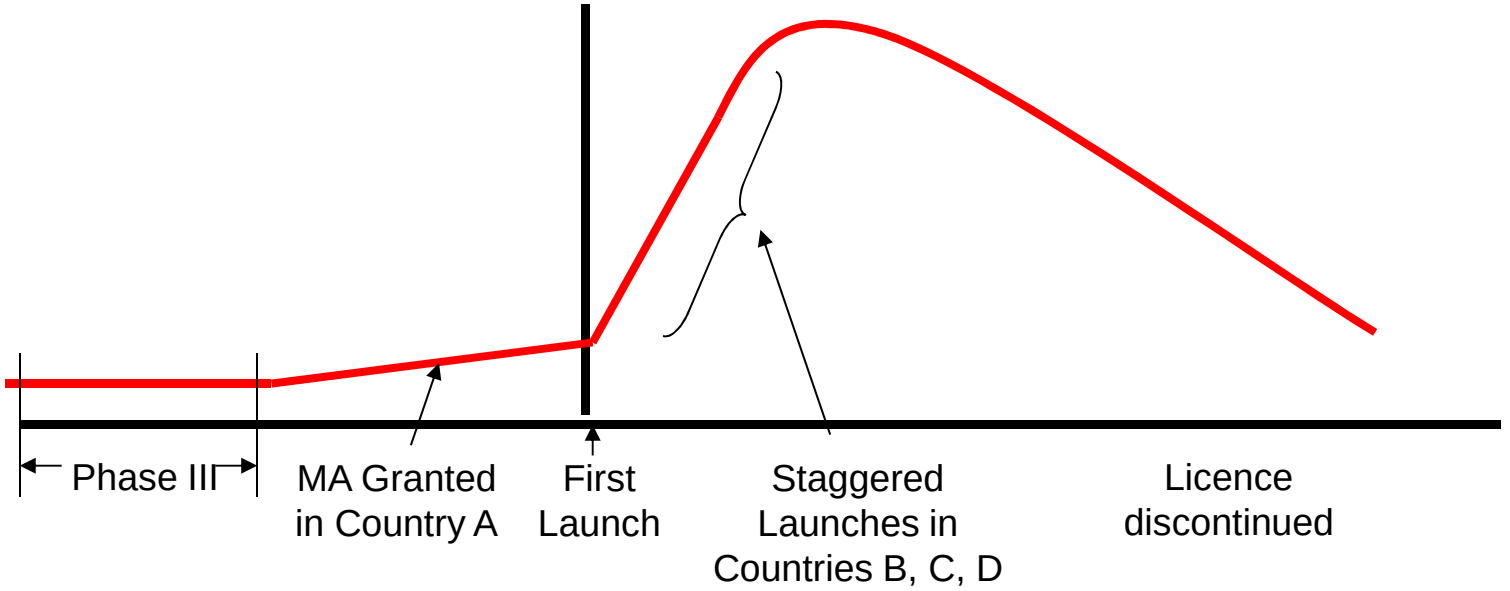
MA is approved

- Final approved MA – gap analysis for any changes from final draft
- Post approval commitments
- Almac Compliance Dossier finalised
- Supply Chain Map finalised

QP Certification and Batch Release

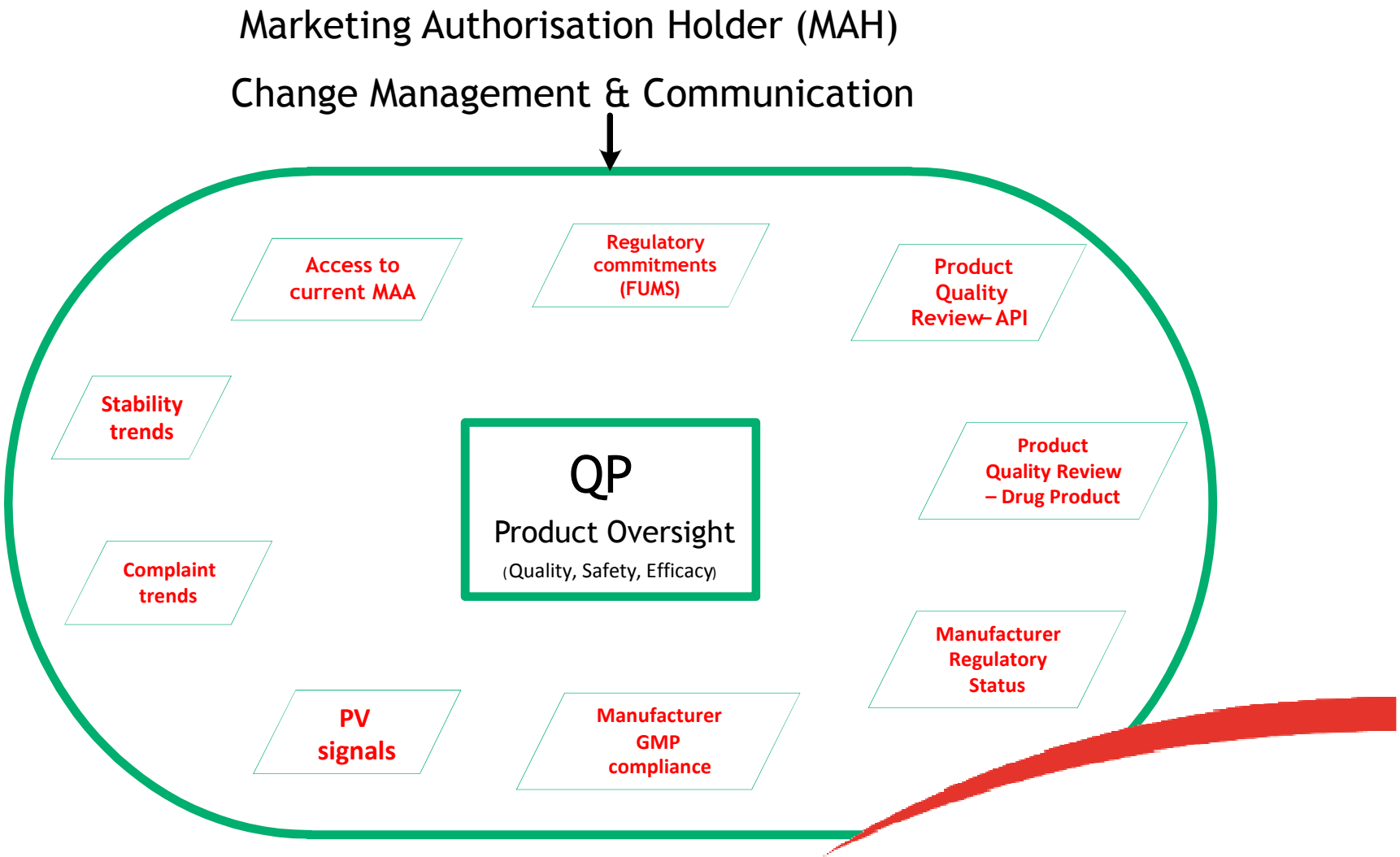
- Every batch must be certified by an EU QP and this can involve extensive reviews of:
  - Manufacturing & packing batch records for compliance with MA and EU GMP
  - Partial Manufacturing Certification (EU Sites)
  - Deviations, OOS results or environmental failures from drug product sites
  - Release test results from EU import testing
  - Temperature conditions during shipment to EU site
  - Any other information relevant to the quality of the batch under review
- Batch Certificate signed and recorded in a register

Quality Considerations – Ongoing Supply



QP Oversight

– QP to oversee Quality, Safety and Efficacy



QP Oversight

- Access to the current Marketing Authorisation
- Regular Quality-Quality Meeting to discuss ‘status’
- Periodic audits of relevant API sites and sites of drug product manufacture, testing and packaging
- Maintenance of non-EU sites compliance status with changes in EU GMPs and regulatory expectations
- Notification of product quality issues which may have implications for product destined for EU market
- Product Quality Reviews/Annual Product Reviews

EU Supply Challenges

1. Non-EU sites not inspection ready or critical findings on EU inspections
2. Under-estimation of project implementation resources
3. Product launch timelines impacted by regulatory questions
4. Contingency planning for launch
5. Actual supply chain failures caused by real world events

Key Messages

Plan key activities well in advance of target product launch date:

- Open communication
- Close collaboration with QP
- Quality Agreement between relevant parties
- Sharing quality critical information and current MA
- Audit of site(s) of API & Drug Product manufacture/testing/packaging
- Regular Quality-Quality Meetings

Thank-you