aqpa
Austrian Qualified Person Association

MRA EU/USA

13. November 2019

Georg Göstl

Background

- Mutual Recognition of GMP-Inspections and Batch Testing
- Fully signed 1 March 2017
- Fully operational 11 July 2019
- During transition all 28 EU inspectorates for human medicines were assessed and accepted by US-FDA
- EU confirmed in June 2017 acceptance of US-FDA GMP-inspections
- As of 11 July 2019, QPs in EU do not need to re-test batches of products covered by the MRA,

BUT

Scope (-> for both: GMP-inspections and Import Testing!)

- Marketed finished pharmaceuticals for human use:

  including tablets, capsules, ointments, injectables, medicinal gases, radiopharmaceuticals, radioactive biological products, herbal products, homeopathic products
- Marketed biological products:
  - Therapeutic biotechnology-derived biological products
  - Allergenic products
- Intermediates
- Active Pharmaceutical Ingredients or Bulk Drug Substance

Products Excluded

- Human blood and plasma (-> plasma-derived products and products containing plasma-derived excipients (e.g. albumin) are not yet in scope!)
- Human tissue and organs
- Veterinary immunologicals
- Advanced therapy medicinal products

<u>Decisions expected on expansion of scope:</u>

- Veterinary medicines: by December 2019
- Vaccines for human use and plasma-derivatives: by 15 July 2022
- Investigational medicinal products: at a later stage

GMP-inspections

- Can be waived for the other geographies, but might be performed upon decisison by the relevant authorities
- Practically:
  - EU-inspectors are reducing their inspections at US-sites
  - FDA-inspectors still perform the majority of EU-inspections
- Regular EU-inspections at US-sites might even be waived in case of non-US-licensed products manufactured at US-sites; provided that US-FDA inspection report contains sufficient conclusion about GMP-compliance (-> case by case decision by EMA)
- If no EU-inspection, there is also no EU-GMP-certificate!
- Alternative for expiring GMP-certificates: request CPP from US-FDA (RA)

Batch Import Testing

- Historically required per Article 51 of EU-Directive 2001/83/EC
- Can now be stopped, provided the rest of EU-Directives and EU-GMP-requirements are still fulfilled and complied with!
  - Product was manufactured in the USA
  - Tests have been carried out in the USA
  - Tests in the USA are performed as per and comply with EU-licensed specifications
  - Each lot is accompanied by a batch certificate in alignment with WHO standard
  - Batch Certificate is issued by the manufacturer certifying that product complies with EU Marketing Authorization(s)
  - Batch Certificate is signed by the person responsible for releasing the batch

-> Basic intention is to accept testing already performed in USA and waive re-testing, not to require transfer of tests to US-sites!

Batch Import Testing

- Consequences before stopping testing in EU:
  - Future testing (if performed in USA): has to comply with approved license dossier in EU -> might require submission of variations (methods, limits, testing site, releasing site, etc.)
  - Only for products manufactured and tested in USA
  - Only for products in scope of the MRA
  - CoA has to comply with WHO-standard
  - Person responsible for release in USA has to be identified (including delegates)
  - Quality Agreements needs to be effective, exactly defining the roles and responsibilities including the identified individuals accepted for signature
  - Release process has to be audited as part of internal audits with specific focus of the MRA
  - Follow Change Control Process

QP-Responsibilites

- ALL QP-responsibilities remain unchanged!
- As e.g. per Directive 2001/83/EC or EU-GMP-Guide and its Annexes
- Including, but not only:
  - QP has to certify each batch in a register (can be based on CoA in case of MRA)
  - Batch complies with Marketing Authorization, GMP and any other legal obligations
  - Regardless how many sites are involved, QP certifying finished products has to take full responsibility
  - QP has to be aware and take into consideration **any** deviations with potential to impact compliance with GMP and/or the MA (including those occured at upstream sites)
  - QP needs to be involved in investigation of quality defects or recalls
  - ALL routine duties of a QP as specified in Annex 16
  - Safety features, where applicable (tamper evidence and unique identifier)
  - The „QP-Declaration Template“ confirming audits at API-manufacturing sites
  - Retention samples of finished product
  - Ongoing stability studies made available to theQP

-> QP cannot delegate responsibility, QP may delegate tasks!