EU GMP Requirements

- Validation -

Bernd Boedecker
GMP Inspectorate of Hannover / Germany

at Turkish Ministry of Health
contact data

Bernd Boedecker
Staatliches Gewerbeaufsichtsamt Hannover
Dezernat 74 (GMP Inspectorate)
Am Listholze 74
D-30177 Hannover

phone: +49 (0)511 / 9096-464
fax : +49 (0)511 / 9096-199
bernd.boedecker@gaa-h.niedersachsen.de
Contents covered

- Legal basis
- Interface regulatory vs. supervisory authorities
- General aspects of qualification & validation
- Qualification of premises and equipment
  - incl. water systems, dedicated systems
- Specific validations
  - Manufacturing process
  - Cleaning
  - Test methods
  - Computer systems
- Recent trends with respect to validation
- Supplier qualification and outsourcing
Definitions

- **Qualification** [EC GMP-Guide, Glossary]:
  Action of proving that any **equipment** works correctly and leads to the expected results.
  The word **validation** is sometimes widened to incorporate the concept of qualification.

- **Validation** [EC GMP-Guide, Glossary]:
  Action of proving, in accordance with the principles of GMP, that any **procedure**, **process**, **equipment**, **material**, **activity** or **system** actually leads to the expected results:

- **Process Validation** [Annex 15 to EC GMP-Guide, Glossary]:
  Documented evidence that the **process**, operated within established parameters, can perform effectively and reproducibly to produce a medicinal product meeting its predetermined specifications and quality attributes

- **(further definitions** see Annex 15)
Legal Frame for Validation

- Regulatory guidances to obtain Market Authorisations (see later)
- Principles of GMP
  - Directive 2003/94/EC (human, incl. investigational)
  - Directive 91/412/EEC (veterinary)
- EudraLex Volume 4 – EC GMP-Guide
  - Part I – Basic Requirements for Medicinal Products [human + vet.]
  - Part II – Basic Requirements for Active Substances (= ICH Q7)
- Annexes, e.g.
  - Annex 15 (Qualification and Validation)
  - Annex 11 (Computerised Systems)
  - Annexes for specific products, e.g. Annex 1 (Sterile), Annex 2 (Bio), etc.
GMP Principles for Validation

- Directive 2003/94/EC (GMP for Human Products)
  - Article 8 No. 3: Premises and equipment to be used for manufacturing operations, which are critical to the quality of the products, shall be subjected to appropriate qualification and validation.

- Article 9 No. 2: When electronic, photographic or other data processing systems are used instead of written documents, the manufacturer shall first validate the systems by showing that the data will be appropriately stored during the anticipated period of storage. …

- Article 10 No. 3: […] any new manufacture or important modification of a manufacturing process of a medicinal product shall be validated. Critical phases of manufacturing processes shall be regularly re-validated.
Integration into Quality System

- EC GMP Guide Part I Chapter 1.1:
  The system of QA should ensure that […]
  - (v) any **validations** are carried out

- EC GMP Guide Part I Chapter 1.2:
  - GMP is that part of QA which […]
  - the basic requirements of GMP are that […]
    (ii) critical steps of **manufacturing processes** and significant changes to the process are validated

- EC GMP Guide Part I Chapter 1.3:
  - Quality Control is that part of GMP which […]
  - the basic requirements of QC are that […]
    (iii) **test methods** are validated

- EC GMP Guide Part I Chapter 1.4:
  the manufacturer and the marketing authorisation holder should evaluate the results of this [**periodic quality**] review and an assessment made whether […]
  any **revalidation** should be undertaken
Responsibilities for Validation

- EC GMP Guide Part I Chapter 2.4: a **Qualified Person** must ensure that each batch has been produced and tested/checked in accordance with the **directives** [...]

- EC GMP Guide Part I Chapter 2.5: The **Head of Production Department** generally has the following responsibilities [...]:
  (v) to ensure that the appropriate **validations** are done

- EC GMP Guide Part I Chapter 2.6: The **Head of Quality Control Department** generally has the following responsibilities [...]:
  (vii) to ensure that the appropriate **validations** are done

- EC GMP Guide Part I Chapter 2.7: The heads of Production and Quality Control generally have some **shared**, or jointly exercised, responsibilities [...]. These may include [...]:
  - **process validation**
  - **plant hygiene** [ cleaning validation]
ERROR: undefined
OFFENDING COMMAND: `~

STACK: