The Quality System for Drugs in Germany

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Steps for a quality system

1996	Decision for a quality system
1999	Quality Management Manual: 17 guidelines
1999	Draft documents for a Quality Assurance System in GMP
2000	Approval of Quality Policy
1999	Implementation and Test Phase
2001	First Revision of Documents; ongoing
2005	Extension of System planned for supervision of - GCP - veterinary medicinal products - wholesalers - pharmacies

Underlying standards

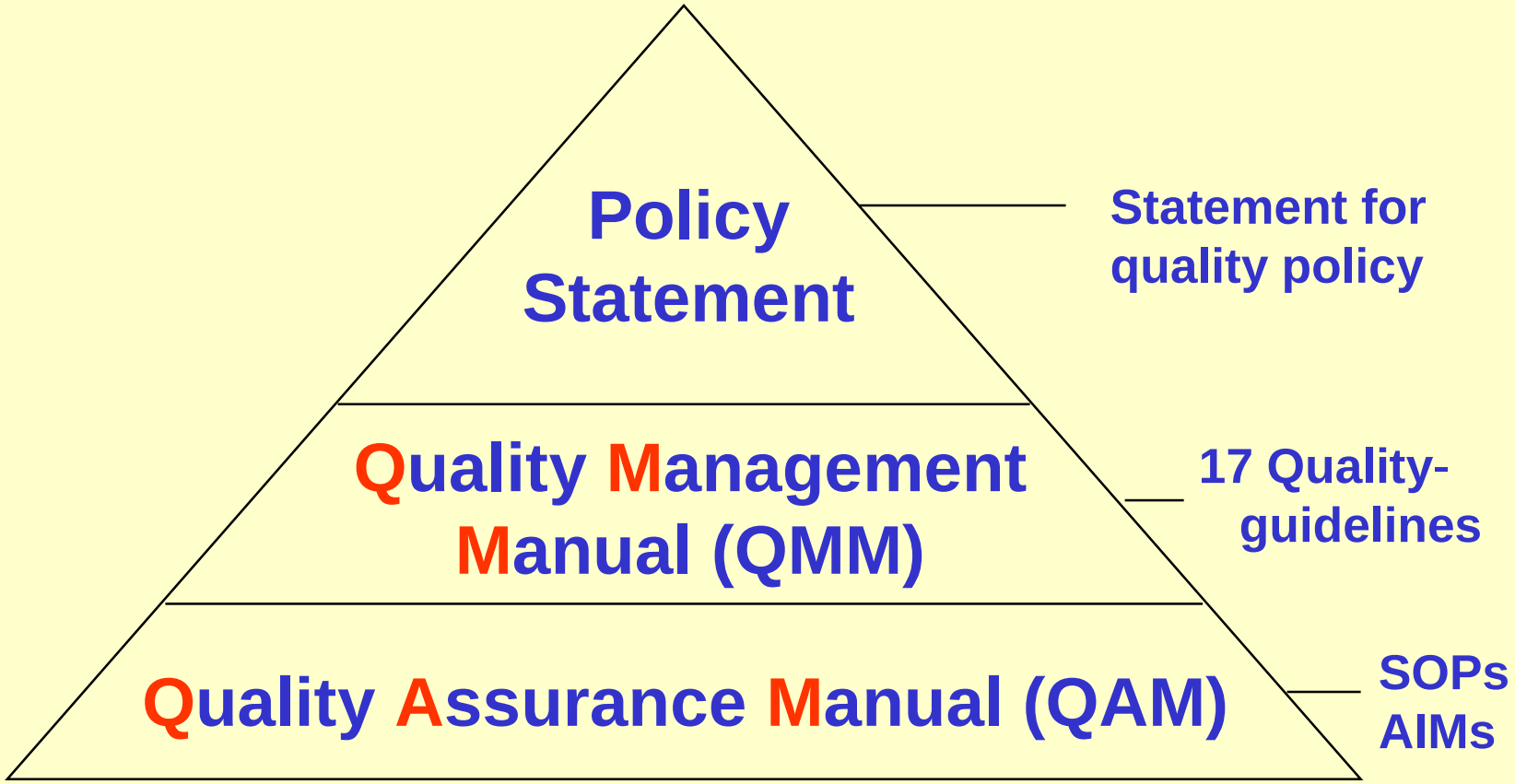
1. PIC/S: Recommendations on quality system requirements for GMP inspectorates
   (PH 7/94; current updated version
   http://www.picscheme.org)
2. European Norms
   EN 45004 (1995)
   EN 45012 (1989)
3. DIN/ISO Norms
   ISO 9002 (1994)
4. Compilation of community procedures on administrative collaboration and harmonisation of inspections (2001)
   (http://pharmacos.eudra.org)

EU- Compilation of Community procedures cover...

- ü Training of inspectors
- ü Manufacturing authorisations
- ü Inspection planning
- ü Inspection performance, follow-up
- ü Inspection report
- ü Action in cases of non-compliance/ defect products (RAS*)
- ü Sampling
- ü Internal Audits

*Rapid Alert System

Structure of Quality System



QM-Manual: Quality Guidelines

- Frame conditions for a detailed quality system
  (responsibilities, organisation and management, personnel, documentation, change control, inspection systems, equipment, quality manuals, transparency, audits, complaint handling, sub-contracting, cooperation, sampling and testing, certificates)

- Decided and approved on political level

Quality Guidelines (1)

1. Responsibility of the upper management
2. Administrative provisions
3. Organisation and management
4. Personnel
5. Documentation
6. Change control
7. Inspection procedures
8. Required equipment / resources
9. Quality assurance manual
10. Confidence building and transparency

Quality Guidelines (2)

11. Internal quality audit and regular checks (management review)
12. Administrative actions for deficiencies and defects
13. Handling of mistakes, complaint management
14. Delegation of tasks
15. Licensing
16. Cooperation
17. Testing of samples

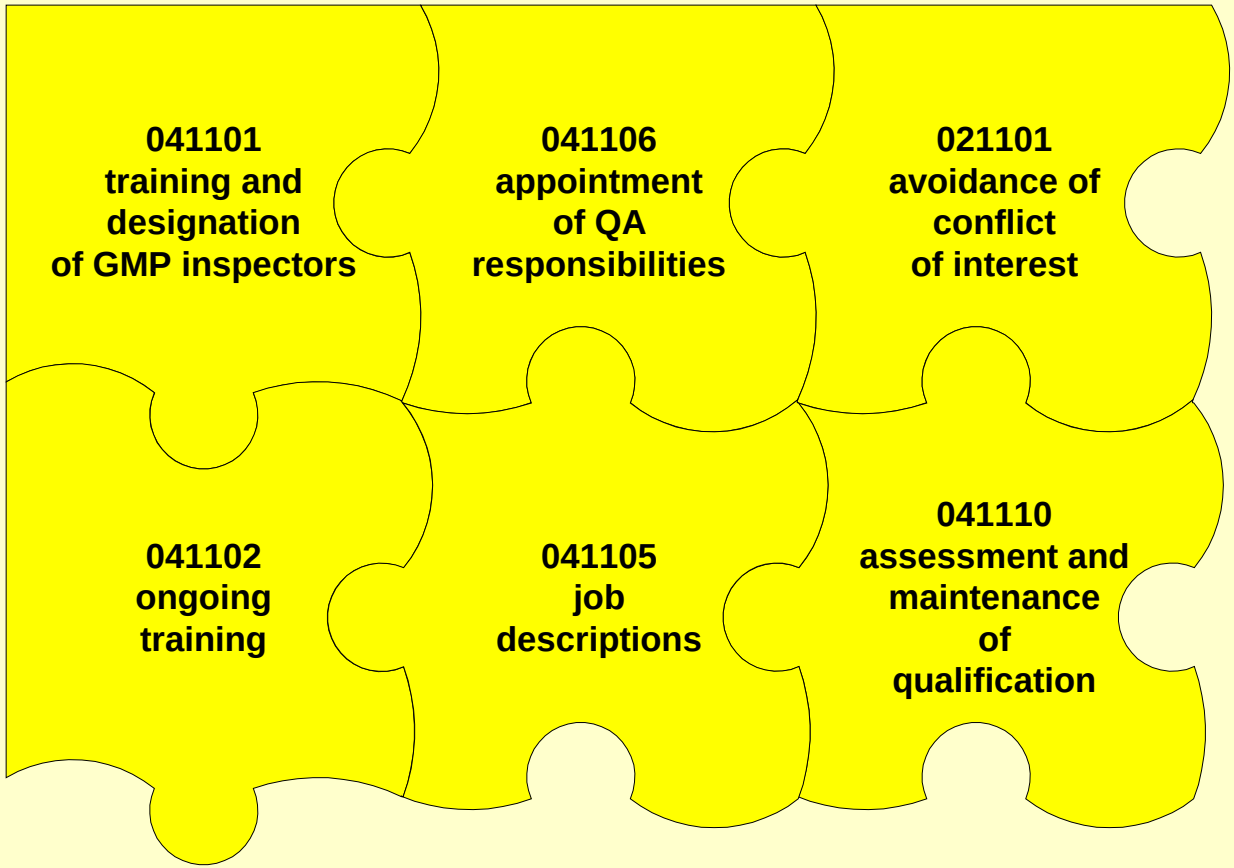
QA-Manual:
SOPs /Aide mémoires

- *32 SOPs (Standard Operating Procedures)*
  (qualification and training of inspectors, manufacturing / import authorisation, inspection performance, inspection planning, certificates, ...)

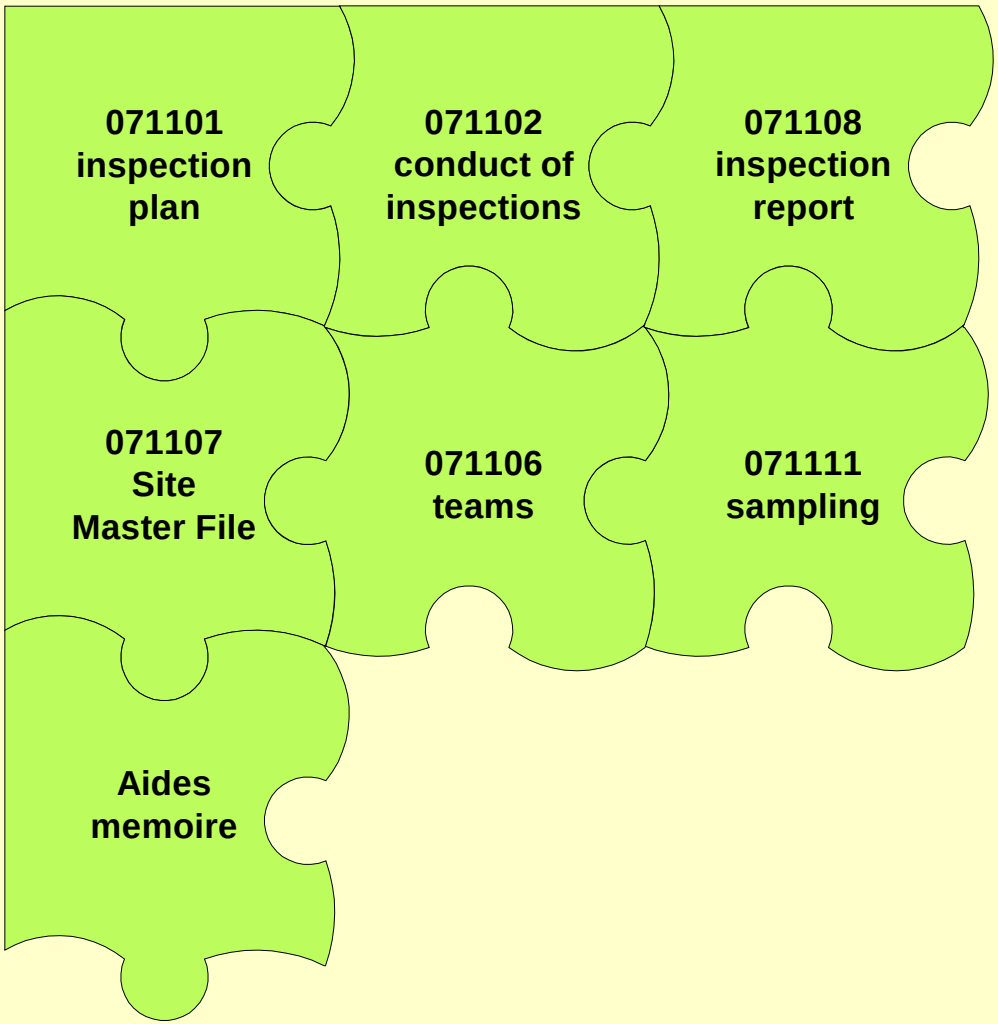
- *8 Aide mémoires*
  (sterile drugs, biotechnology, computerized systems, blood products, active ingredients, ...)

- *Developed on an expert level*

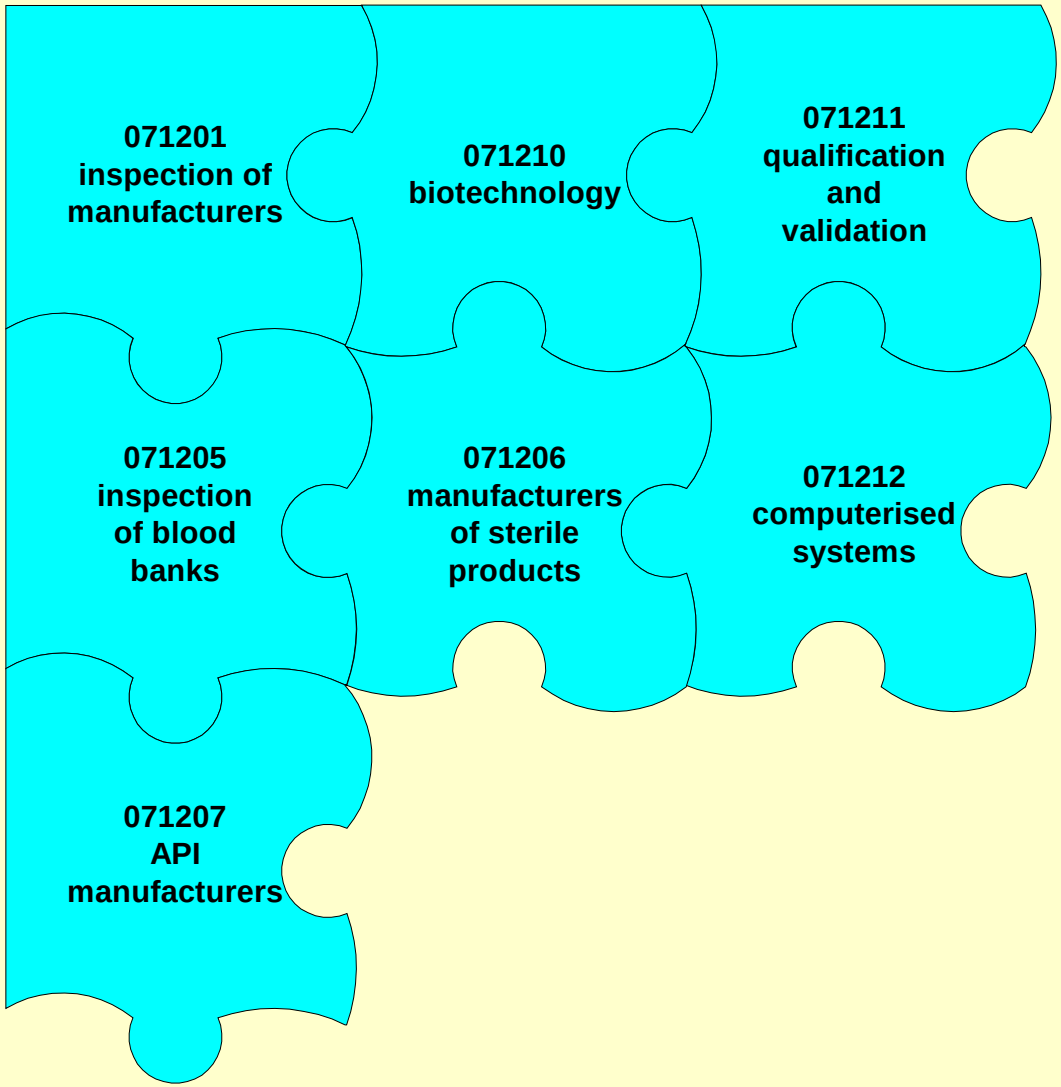
Specific Procedures
Staff



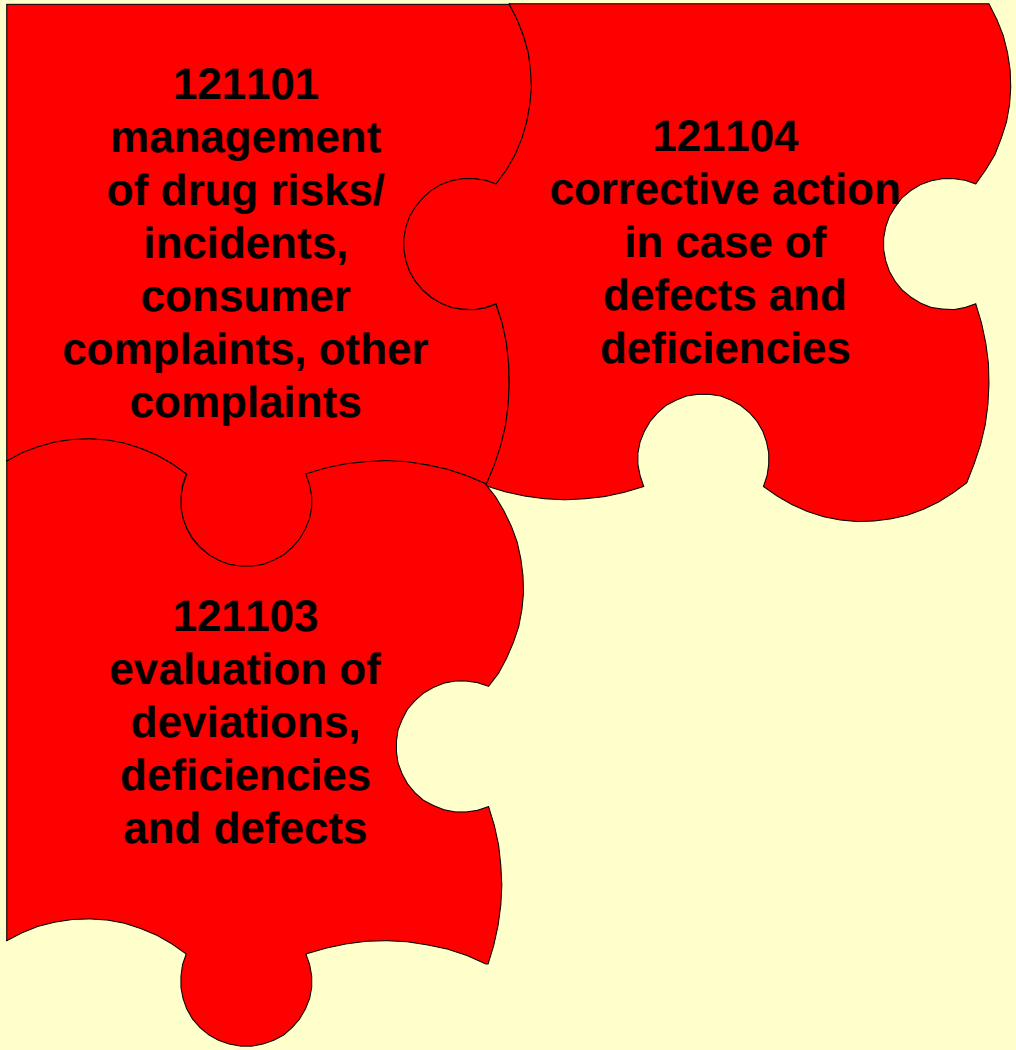
Inspections



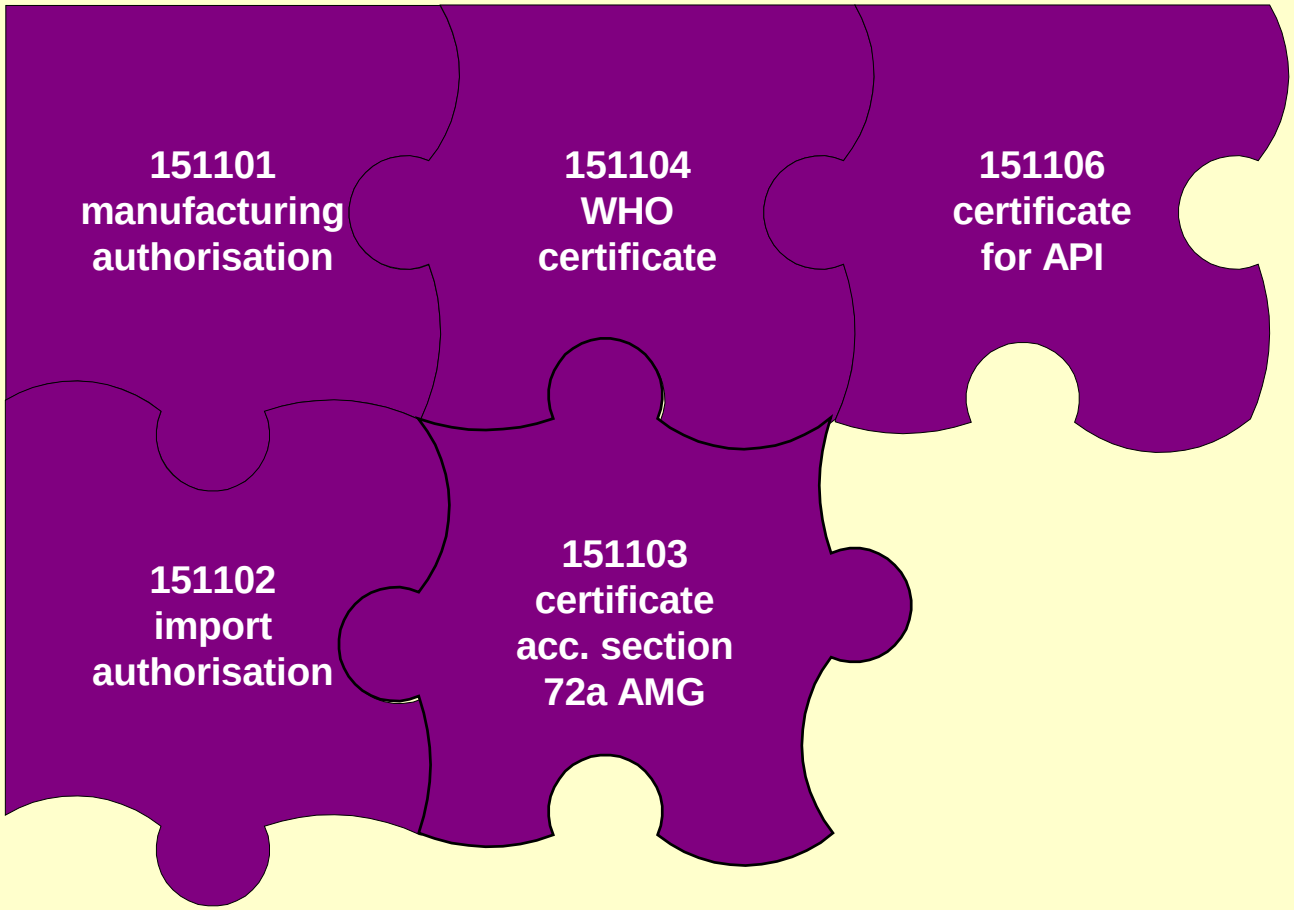
Aides mémoire for Inspections



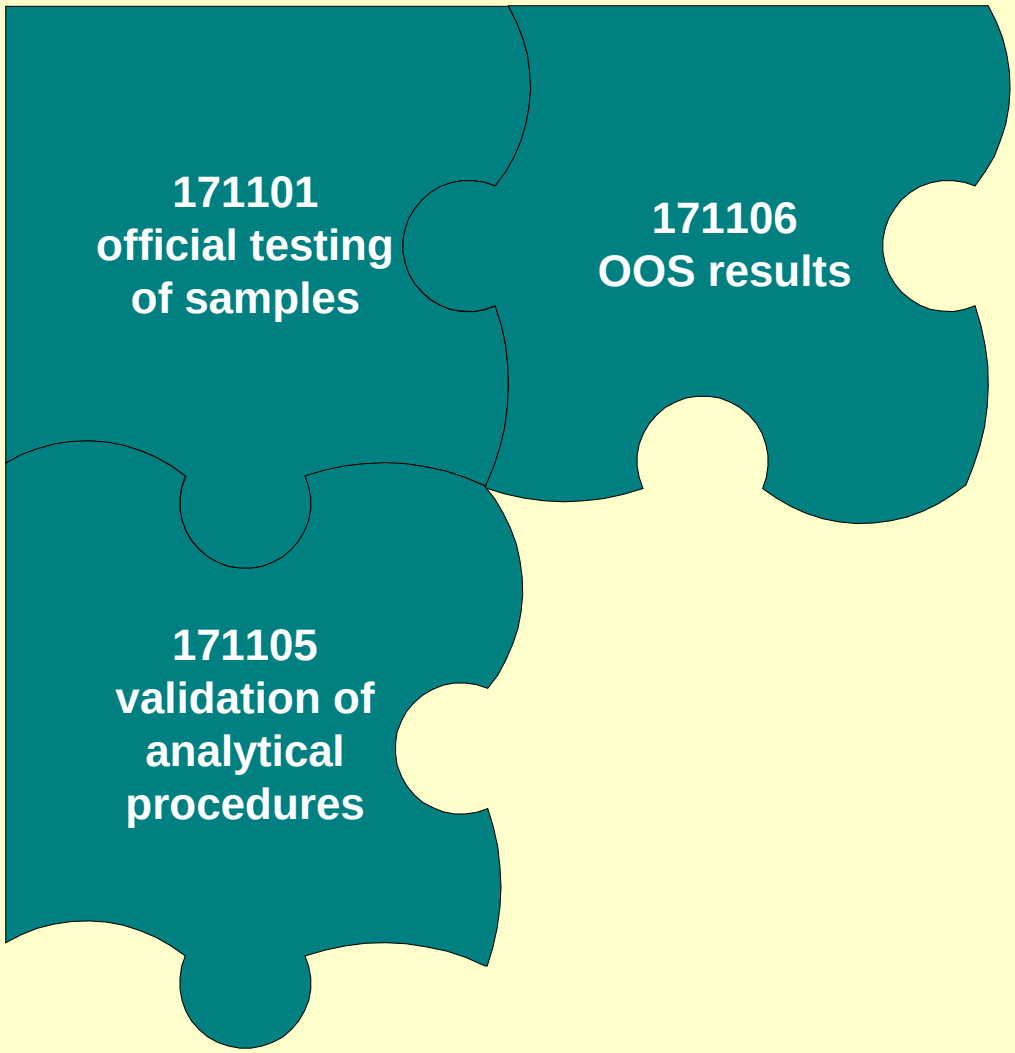
Quality Defects



Authorisations/Certificates



Drug Testing



041101 Training and Designation of GMP Inspectors

1. Basic qualification: pharmacists
   veterinarian (only for vet. prod.)
2. Baseline Training: 2 years in an inspectorate
   of which 6 months may be in
   OMCL, Länder ministry,
   Federal Ministry, quality lab (ZLG)
3. Theory: as in „Compilation of
   community procedures...“
4. Practical training: at least 10 joint inspections
   with senior inspector
5. Final exam inspection
6. Formal designation

041102 Ongoing Training

1. At least 10 days per year, e.g.:
    - Conferences (e.g. PIC/S , commercial conferences)
    - German annual conference
    - Expert group trainings
    - Joint inspections/ joint visits
    - Local SOP training sessions
2. Formal documentation in personal file

041110 Assessment and Maintenance of Qualification

- Every 5 years by head of inspectorate
- Assessment may be covered by:
  - Quality audit
  - Evaluation of inspection reports
  - participation in inspections
- Possible actions:
  - specific training
  - participation in inspections in other inspectorates
  - suspension or revocation of designation

SOP 07111102: Sampling

- Sampling plan by OMCL in cooperation with inspectorate
- Analytical evaluation of „risk products“ within 5 years after approvals
- „Risk products“:
  - New chemical entity
  - API with narrow therapeutic range
  - API with low stability
  - Dosage form with specific technological properties/ problems

Audit Systems 111101: Audits

1.	Subject:	Inspectorates
2.	Biannual cycle:	Organisation Procedures Quality System
3.	Auditors:	at least 2 at least 1 GMP inspector
4.	Corrective Action :	to be proceeded to management to be evaluated by auditors

Inspections of API* manufacturers in Germany

Legal requirements:

- Under scope of centralised procedure
- National level:
  - only APIs of human and animal origin; biotec APIs
  - After publication of Ordinance: all APIs

Practical implementation

- Voluntary inspections of API manufacturers
- Voluntary 3rd country inspections

* Advanced Pharmaceutical Industry

Conclusions:
What we learnt about the process...

- to give enough time for discussions on all levels
- to make sure that all parties involved have enough time to make contributions
- to make sure that contributions are clearly evaluated
- to allow for 70 % accuracy at the beginning
- to allow for a pilot phase in order to collect practical experiences
- to intensively monitor the implementation phase
- to adjust immediately where necessary

Thank
you
for your
attention !