
Tasks of ZLG

Quality System

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Quality System

- Established to comply with the MRAs
- To show equivalency of the inspection systems of the German Länder (EU, PIC/S)
- In accordance with the requirements of the European *Compilation of Community Procedures*
<http://www.emea.europa.eu/Inspections/GMPCompproc.html>
- National Regulation: AMG VwV

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Quality System - Who has to comply?

...for processes with medicinal products for human and veterinary use

- Länder Ministries of Health (Pharmaceutical Divisions)
- Competent Authorities (Inspectorates)
- OMCLs
- ZLG

...for all documents of the system

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Quality System – Operational Level

2 Pillars

- Elaboration of Guidance → Expert groups
- Maintenance → ZLG

- Assessement of Compliance/ Monitoring
→ Expert groups 01/16 (hum/vet)
- Administration → ZLG

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Quality System – Operational Level

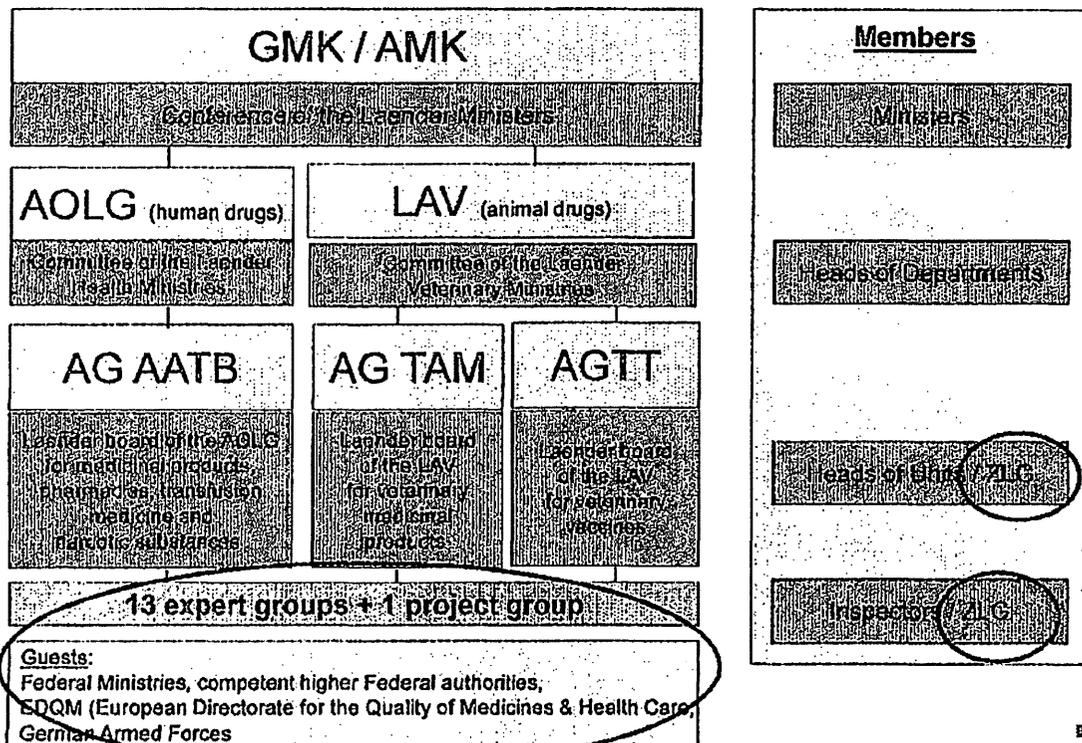
First Pillar

Elaboration of Guidance

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Elaboration of QS-Documents - involved bodies



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Expert Groups – Instruments for Collaboration and Coordination

- regular expert group meetings (twice a year)
- share information and experience
- availability of topics for discussion, results and documents on www.zlg.de
- develop SOPs and Aides mémoire
- regular trainings
- annual national conference including GMP workshops

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Expert Groups (German: **Expertenfachgruppe**)

- | | |
|------------------------------------|--|
| EFG 01: quality assurance | EFG 02: inspections, GMP-Guideline |
| EFG 03: sterile medicinal products | EFG 04: biotechnology and tissues |
| EFG 05: clinical trials | EFG 06: blood ad blood products |
| EFG 07: active substances | EFG 08: OMCLs |
| EFG 10: qualification, validation | EFG 11: computerized systems |
| EFG 12: radiopharmaceuticals | EFG 13/14: veterinary medicinal products/medicated feeding stuff |
| | EFG 16: veterinary vaccines |

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Quality system covers

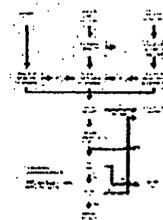
-
- Training of inspectors
 - Manufacturing authorisations
 - Inspection planning
 - Inspection performance, follow-up
 - Inspection report
 - Action in cases of non-compliance / defect products (RAS)
 - Sampling
 - Internal Audits

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Quality Documents

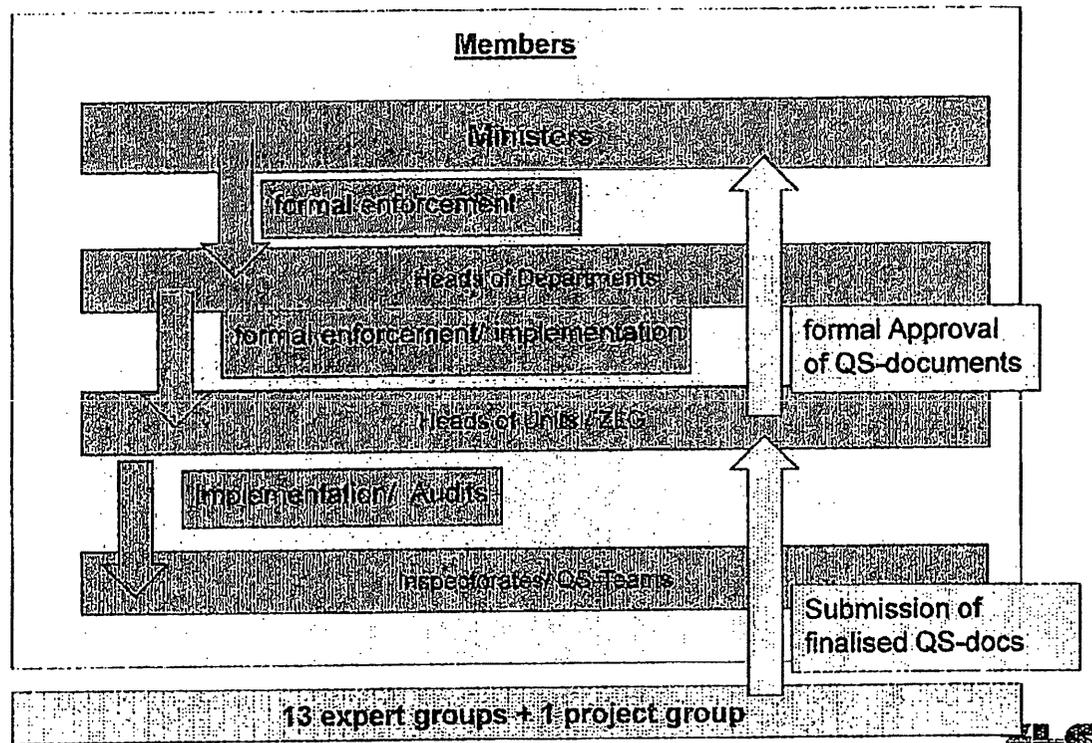
-
- developed on an expert level
 - Members of expert working groups are inspectors with special expertise and Experience
 - Each Region (Land) shall ensure to send a member
 - formally decided by Laender boards (representatives of Laender ministries)
 - Set into force by Laender ministries
 - Implemented by authorities on regional level
 - Note: no automatic enforcement on a national level
 - published on www.zlg.de



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Enforcement/ Implementation of QS Standards



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Quality system- processing of QS-documents

- Elaboration of SOP's by leading EFG
- Involvement of concerned parties
- Final approval through leading EFG
- Formal assessement through ZLG
- Circulation to and authorisation by political councils (vet/hum)
- Release ZLG and circulation of final authorised Documents
- Enforcement/implementation of guidance documents through authorities of the Laender
- Publication

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Quality System – Operational Level

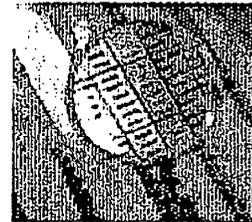
Second Pillar Maintenance and Assesement

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National Auditsystem

- SOP 111102
- **Audit teams** (EG 01, inspectors)
- Involving staff / inspectorates from several Laender
- **(QS-Teams → within each Land)**
- Scope:
 - Organisation
 - Personnel / Qualification / Training
 - Quality System
 - Inspection Procedures
 - Documentation
 - Rapid Alert Handling



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EU Joint Audit Programme (JAP)

- Audits between the European authorities hum/vet in EEA
- to verify the implementation of relevant provisions of European Directives into national laws, authorisation / licensing system for manufacturers, GMP compliance certification, administration of inspections, inspectorate, resources, complaints, rapid alerts including laboratory support, enforcement and internal quality assurance.

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Scope of JAP Audits

- Quality system, including implementation of Compilation of Community Procedures
- Implementation of Legislation related to the GMP supervision system
- Authorisation / licensing system for manufacturer
- GMP guidance
- GMP compliance certification
- Administration of inspections (e.g. frequencies, resources, procedures)
- Qualifications and training of inspectors
- Inspections (planning, performance, reporting and follow-up system)
- Complaints
- Rapid alerts
- Obligations as EU Member State
- Internal audits
- Observed inspections (if carried out)

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Quality System - Coordination

ZLG-tasks on an operational level

- Monitoring
- Coordination of revision process (among EFG'en)
 - identify interfaces, initiate discussions between expert groups
- Administration of SOP-versions
 - Version control
 - Archiving
 - Formal check
 - Administrative approval process
 - Publication
- Compliance check with view to international regulations/ agreements

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Quality System - Coordination

ZLG-tasks on a political and administrative level

- Information of all relevant stakeholders (operational and political level)
- Coordination of contentwise issues
- Exchange of information international
- Coordination international

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Quality System – system monitoring

ZLG-tasks on internal level

- Monitoring, systematic reviews of QS-Laender and ZLG-QS
- Revisions of QS-Laender and ZLG-QS
- Interface QS-Laender, QS internal (segregated systems)
- Transfer of international regulations/ agreements in national QS

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Thanks for Your Attention



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Quality System for the Surveillance of Medicinal Products

Melanie Gräf

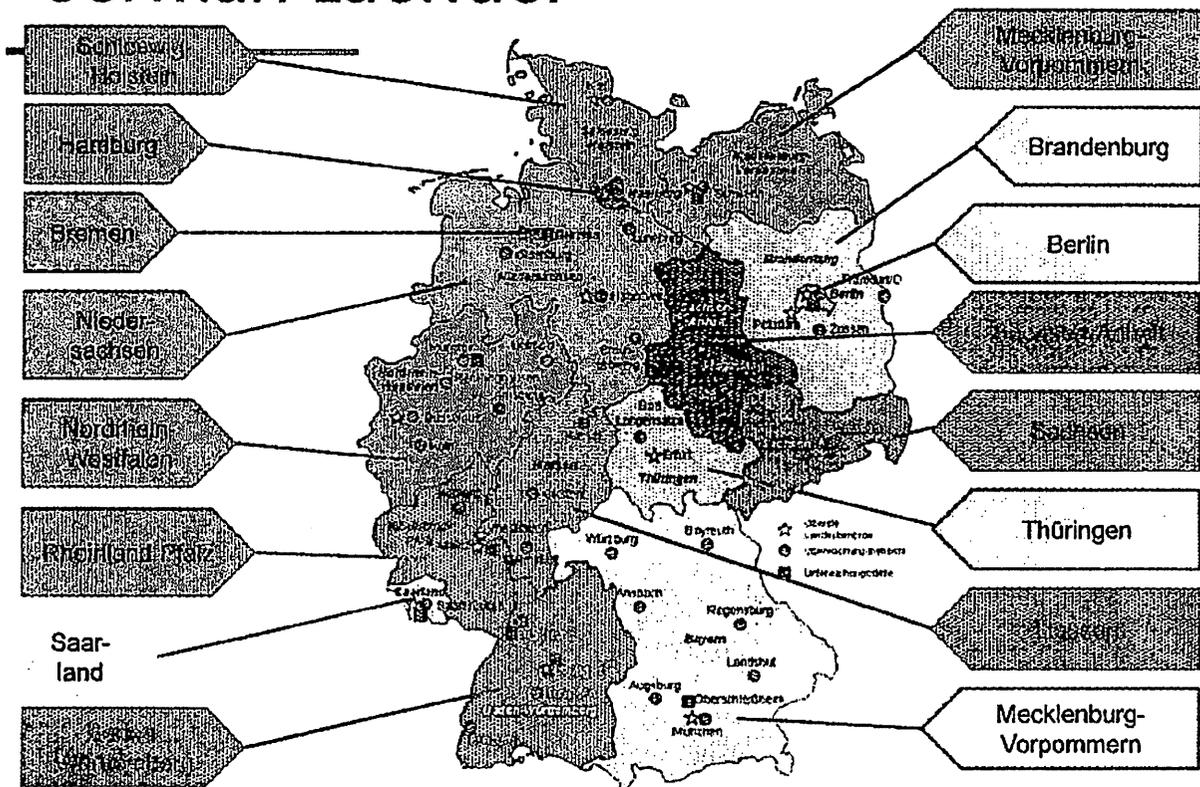
Central Authority of the Laender for Health Protection with regard to Medicinal Products and Medical Devices

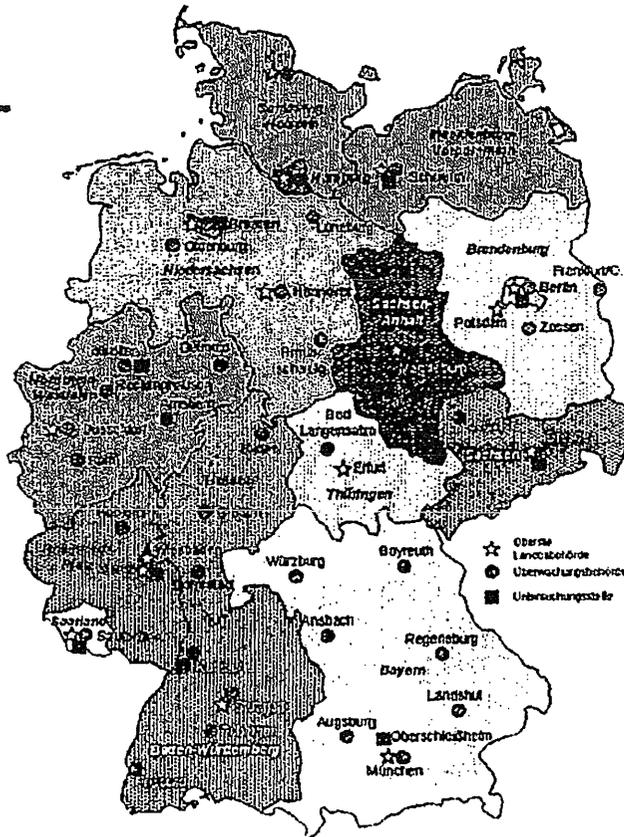


April 2011

www.zlg.de

German Laender





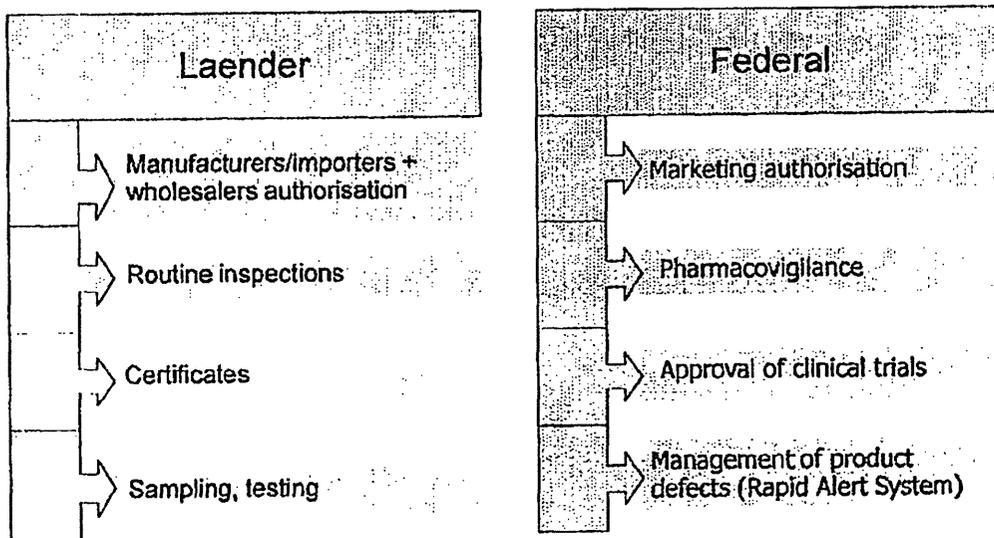
☆ Highest Authorities of the Laender

● Surveillance Units / Inspectorates

■ OMCL = Official Medicines Control Laboratories



Drug-Law



History

1. Case of HIV contaminated blood in the early nineties
2. Political decision for a
 - Quality system
 - Qualified specialisation of inspectors
 - Central Coordination Unit (ZLG)
3. Improvement of exchange between the Laender:
 - Expert Groups
 - Inspection cooperation networks

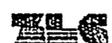
55



Quality System

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- To show equivalency of the inspection systems of the German Laender (EU, PIC/S)
- In accordance with the requirements of the **European Compilation of Community Procedures**
- National Regulation: AMG VwV

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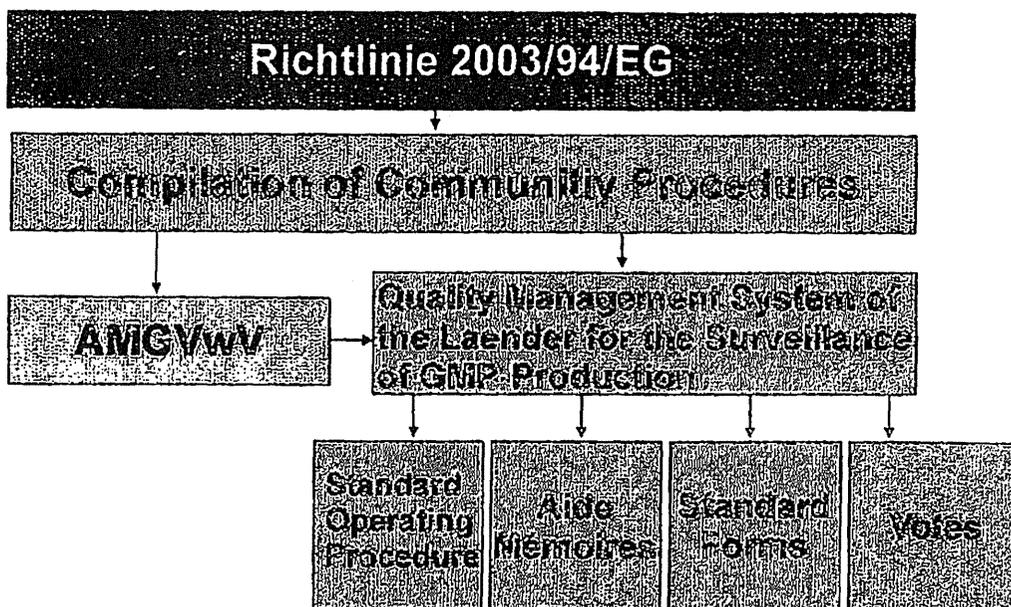
CoCP covers

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

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Medicinal Products Act § 1: It is the purpose of the present Act to guarantee, in the interest of furnishing both human beings and animals with a proper supply of medicinal products, safety in respect of the trade in medicinal products, ensuring in particular the quality, efficacy and safety of medicinal products in accordance with the following provisions.



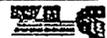
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Expert Groups

EG 01: quality assurance	EG 02: inspections
EG 03: sterile medicinal products	EG 04: biotechnology and tissues
EG 05: clinical trials	EG 06: blood products
EG 07: active substances	EG 08: OMCLs
EG 10: qualification, validation	EG 11: computerized systems.
EG 13: veterinary medicinal products	EG 14: medicated feeding stuff
EG 15: medicinal gases	EG 16: veterinary vaccines

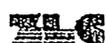
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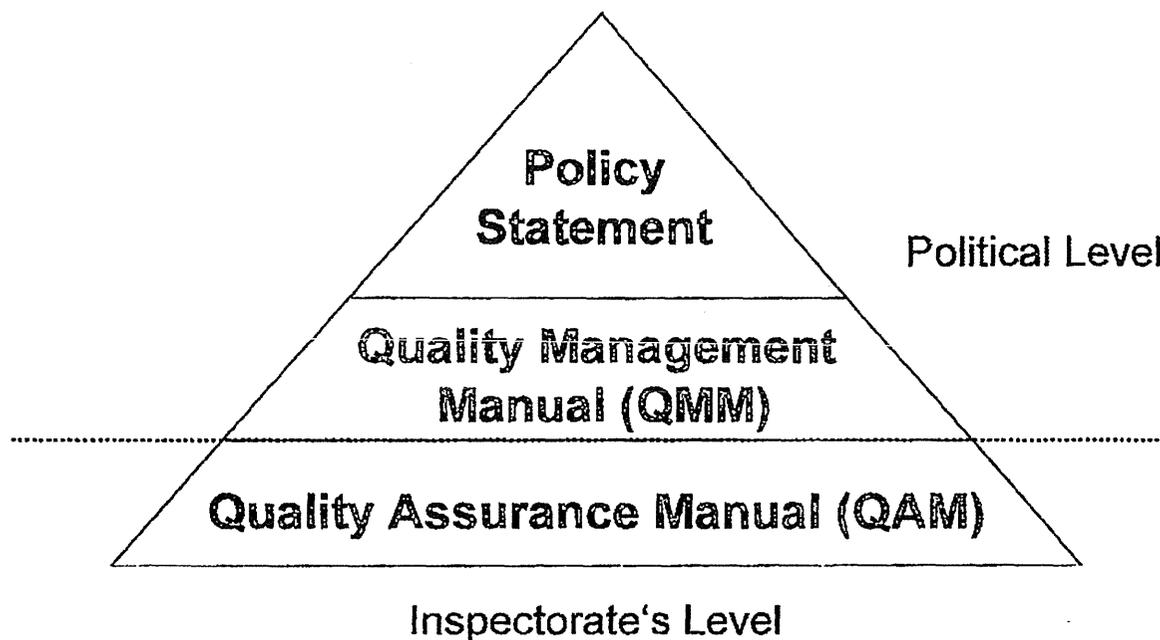
Expert Groups – Instruments for Collaboration

- Regular Expert Group meetings
- Experts of GMP inspectorates + experts of higher Federal authorities
- Share information and experience
- Availability of topics for discussion, results and documents published on www.zlg.de
- **Develop documents for the Quality System for the Surveillance of Medicinal Products**
- Regular trainings
- Annual national conference including GMP workshops

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Structure of Quality System



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Quality Management Manual

Content

17 Guidelines of Quality Assurance :

- Decided and approved on a political level
- Frame conditions for a detailed quality system

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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

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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

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Quality Assurance Manual

- ▣ Developed on an expert level
- ▣ Decided by Laender boards
(representatives of Laender ministries)
- ▣ ZLG-Database
- ▣ Published on the ZLG-Website www.zlg.de
- ▣ Regular revisions of all documents
(developing new versions)
- ▣ Additional documents in preparation

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Standard Operating Procedures

Currently 55 SOP

Examples:

- ▣ Training, nomination, further education and assessment of qualification of GMP inspectors
- ▣ Appointment of QA Responsibilities, establishing of a QA Team
- ▣ Structure and Format of QA Documents common in all Laender
- ▣ Work on and Authorisation of QA Documents common in all Laender
- ▣ Regulation on changes and deviations

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SOP Examples

- Preparation, conduct and assessment of inspections in the field of GMP
- Organisational aspects of preparation, conduct and assessment of third country inspections in the field of GMP
- Format of inspection reports
- Inspections of clinical trials
- Supervision of house dispensary of veterinarians
- Annual report on drug supervision
- Decision making on granting wholesale distribution authorisations according to sect 52a AMG

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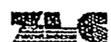
Aides Mémoire

Currently 11 Aides Mémoire *Guidelines for Inspections*

Examples:

- Inspection of manufacturers
- Mechanised packaging of medicinal product for patient single use
- Inspection of blood banks/plasmapheresis centers
- Inspection of sterile manufacturers
- Inspection of manufacturers of Active Pharmaceutical Ingredients
- Biotechnology and genetical engineering

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Votes and Standard Forms

Currently 12 Votes

Advice by Expert Group

Examples:

- Requirements on electronic signatures
- Requirements on storage of electronic data

Currently 10 Standard Forms

Which are part of a SOP, but constitute an own QA document

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Who has to comply?

For processes with medicinal products for human and veterinary use:

- Laender Ministries of Health (Pharmaceutical Divisions)
- Competent Authorities (Inspectorates)
- OMCLs*
- ZLG **

* Existing local QA-Systems in OMCLs linked to a selection of documents of Laender Quality System

** Implementation within internal QM-System

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