Technical Proceeding

- Elaborated by Expert Groups
- Decided by Laender boards
- ZLG Database – Publication on ZLG Website
- Quality Officers, Quality teams within the Inspectorates and Laender
- Implementation within each single Inspectorate
- Auditsystem to evaluate suitabilty of the System and Compliance with it
- Regular reporting to Laender Boards

Monitoring

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- Implementation within each single inspectorate
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National Audit System (1)

- SOP 111102 Conduct of Internal Audits
- Audit teams (EG 01 and EG 16, inspectors)
- Involving staff / inspectorates from several Laender

National Audit System (2)

- Scope:
  - Organisation
  - Personnel / Qualification / Training
  - Quality System
  - Inspection Procedures
  - Documentation
  - Rapid Alert Handling

EU Joint Audit Programme (JAP)

- Audits between the European authorities hum/vet in European Economic Area (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.

Scope of JAP Audits (1)

- Quality system, including implementation of Compilation of Community Procedures
- Implementation of Legislation related to the GMP supervision system
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- GMP compliance certification
- Administration of inspections (e.g. frequencies, resources, procedures)

Scope of JAP Audits (2)

- 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)

Tools to Demonstrate the System

- Table to match the requirements of CoCP and AMGVwV with the existing documents
  - ➢To present the system e. g. in the JAP
  - ➢To identify need for action
- „Quality Site Master File“
  - ➢Audit Checklist of the PIC/S Joint Reassessment Programme
  - ➢Model answers for German inspectorates

Thank you for your Attention!

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Quality System for the Surveillance of Medicinal Products

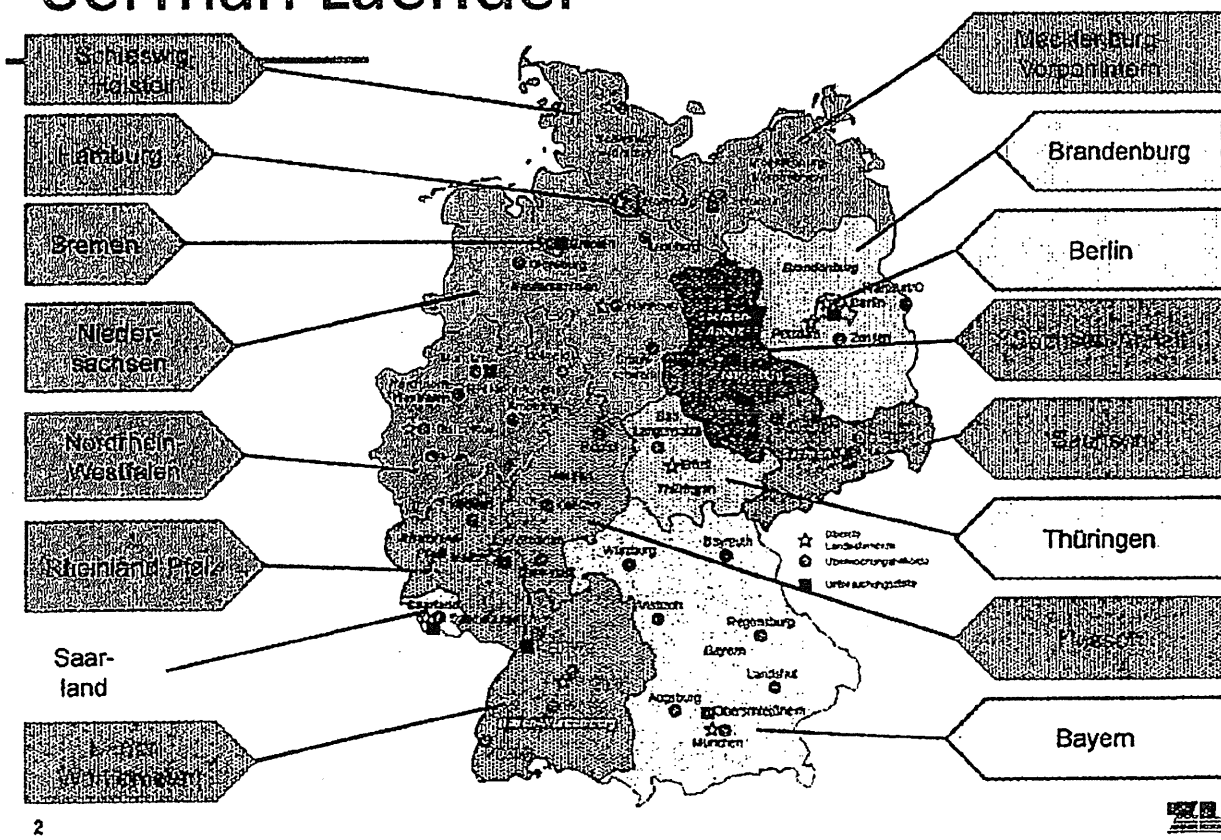
Melanie Gräf

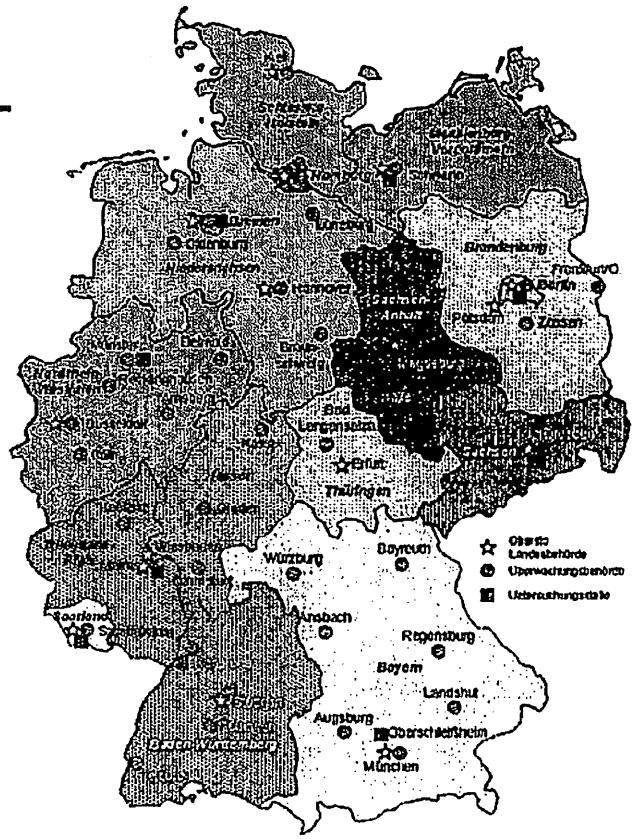
Central Authority of the Laender for Health Protection with regard to Medicinal Products and Medical Devices

April 2011

www.zlg.de

German Laender





☆ Highest Authorities of the Laender

Surveillance Units / Inspectorates

OMCL = Official Medicines Control Laboratories

3

Drug-Law

Laender	Federal
Manufacturers/importers + wholesalers authorisation	Marketing authorisation
Routine inspections	Pharmacovigilance
Certificates	Approval of clinical trials
Sampling, testing	Management of product defects (Rapid Alert System)

4
2

History

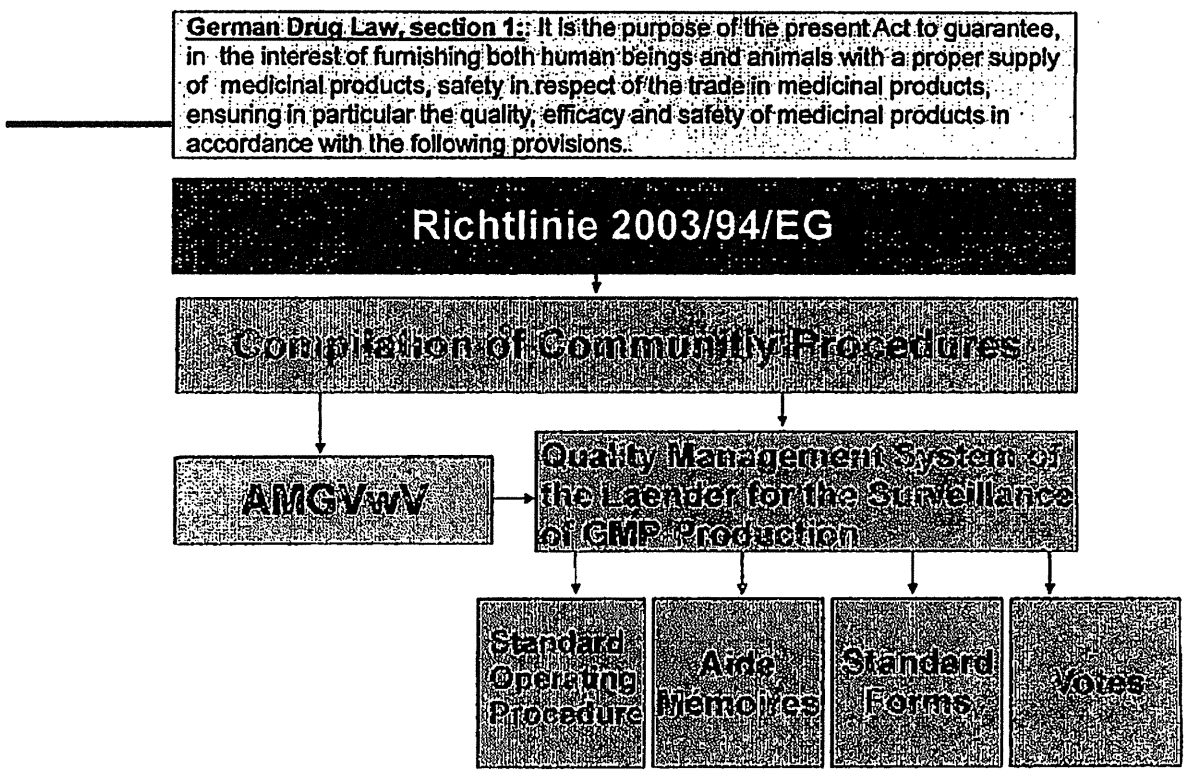
1. Case of HIV contaminated blood in the early nineties
2. Political decision for a
   - Quality system
   - Qualified specialisation of inspectors
   - Central Coordination Unit (ZLG)
3. Improvement of exchange between the Laender:
   - Expert Groups
   - Inspection cooperation networks

Quality System

- Established to comply with the MRAs
- 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 Pocedures**
- National Regulation: AMGVwV (administrative regulation)

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



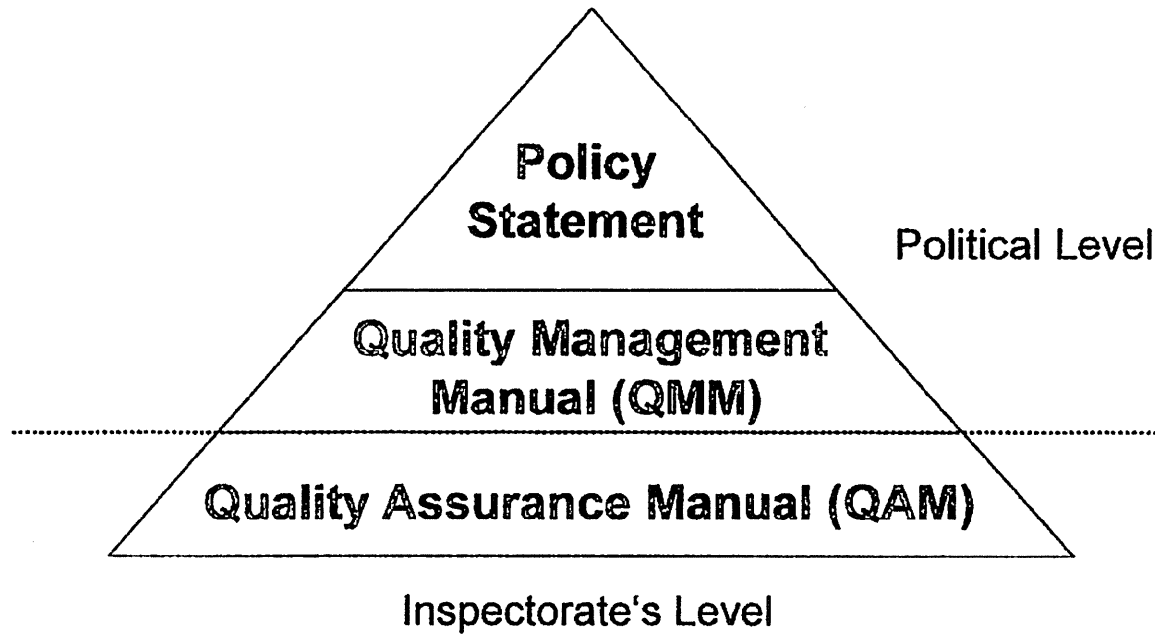
Expert Groups

EG 01: Quality Assurance	EG 02: Inspections
EG 03: Sterile And Aseptically Manufactured Medicinal Products	EG 04: Biotechnology and Tissues
EG 05: Clinical Trials	EG 06: Blood / Blood Products
EG 07: Active Pharmaceutical Ingredients	EG 08: Drug Analysis
EG 10: Qualification, Validation	EG 11: Computerized Systems
EG 12: Radiopharmaceuticals	EG 13/14: Veterinary Medicinal Products / Medicated Feedingstuffs
EG 16: Veterinary Vaccines	

Expert Groups – Instruments for Collaboration

- Regular Expert Group meetings
- Experts of GMP inspectorates + experts of higher Federal authorities
- Share information and experience
- 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

Structure of Quality System



Quality Management Manual

Content

17 Guidelines of Quality Assurance :

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

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

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

ZLG

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

ZLG

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

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

Votes and Standard Forms

Currently 12 Votes
Advice by Expert Group

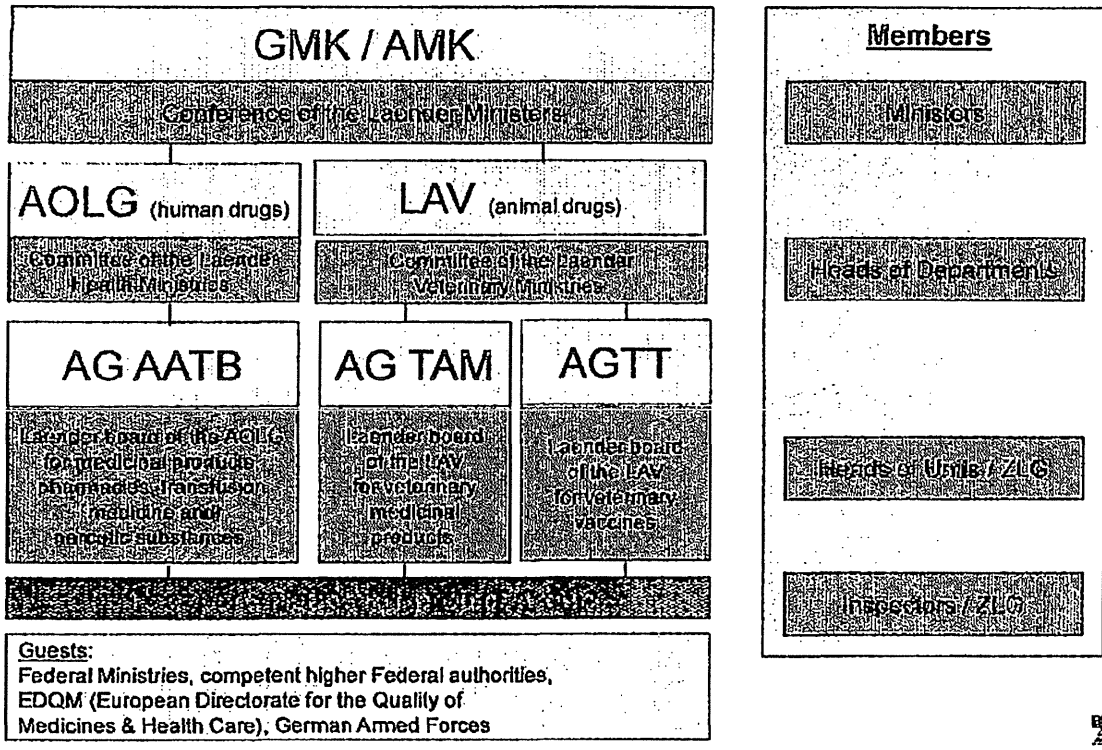
Examples:
- Requirements on electronic signatures
- Requirements on storage of electronic data

Currently 10 Standard Forms
Which are part of a SOP, but constitute an own QA document

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

Laender Boards / Committees



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