

# Sneak Peek

*Advanced Strategies  
and Future Trends  
in GMP Auditing*

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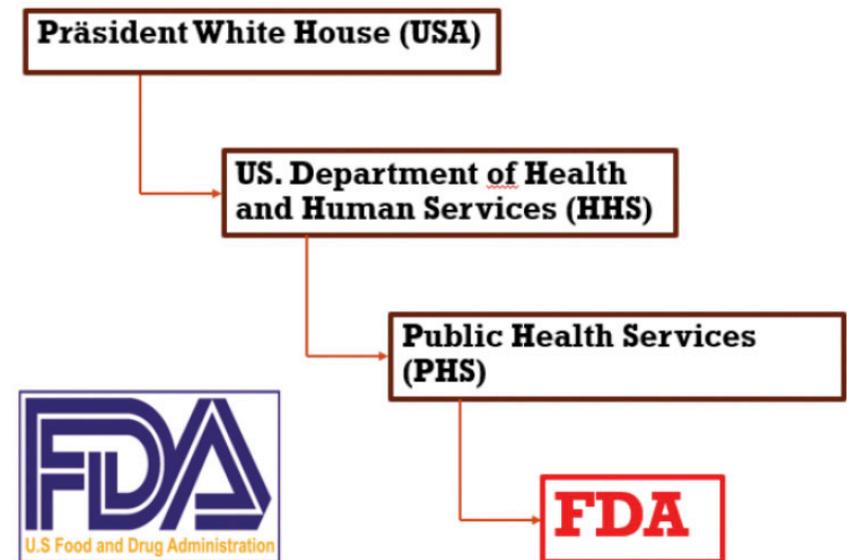
**SYMMETRIC**

# GMP AUDITS

## WHAT SHOULD BE CONSIDERED REFERRING TO AUTHORITY INSPECTION?

### Food And Drug Administration

- Health authority of the USA
  - Strong dependence on political decisions
  - About 3.000 employees / 1.500 auditors
  - Responsible for the approval and the surveillance
- Strict authority
  - Do not let them wait too long onto documents
  - No confusion
  - Fast suspected fraud
  - Well organised and fast creating clusters referring to topics
  - Very interested and open to new technologies



Bildquelle:  
<http://www.pharmamicroresources.com/2017/09/analysis-of-fda-warning-letters.html>

## QUESTION 3

What is in the focus of an external audit?

- A) CMOs
- B) CLaOs
- C) Both CMO and CLO



# EXAMPLE 2: GMP-AUDIT REPORT

## STANDARDISATION OF THE MAIN PART

Audit Report

Section	OK	n/a	AR	Section	OK	n/a	AR	Section	OK	n/a	AR	Section	OK	n/a	AR
<b>2 Quality Management</b>				4.43				6.3				8.21			
2.1				4.5				6.30				8.3			
2.11				4.6				6.31				8.30			
2.12				4.60				6.4				8.32			
2.13				4.7				6.40				8.33			
2.14				4.70				6.41				8.34			
2.16				4.71				6.5				8.35			
2.17				4.72				6.50				8.4			
2.18								6.51				8.41			
2.2				<b>5 Process Equipment</b>				6.52				8.43			
2.21				5.1				6.6				8.44			
2.22				5.10				6.60				8.45			
2.3				5.11				6.61				8.46			
2.4				5.12				6.7				8.47			
2.40				5.13				6.70				8.5			
2.41				5.14				6.71				8.51			
2.5				5.15				6.72				8.52			
2.50				5.16				6.73				8.53			
				5.2				7.1				9.1			
				5.20				<b>7 Materials Management</b>				<b>9 Packaging and Identification Labelling of APIs and IM</b>			
				5.21				7.10				9.1			
				5.22				7.11				9.10			
3.10				5.24				7.12				9.11			
3.11				5.25				7.13				9.12			
3.12				5.26				7.14				9.2			
3.2				5.3				7.2				9.20			
3.21				5.30				7.20				9.21			
3.22				5.31				7.21				9.22			
3.23				5.32				7.22				9.3			
				5.33				7.24							
								7.3				9.31			
4.10				5.35				7.30				9.32			
4.11				5.4				7.31				9.33			
4.12				5.40				7.33				9.34			
4.13				5.41				7.34				9.36			
4.14				5.42				7.35				9.4			
4.15				5.43				7.4				9.40			
4.16				5.44				7.40				9.41			
4.2				5.45				7.41				9.42			
4.20				5.46				7.42				9.43			
4.21				5.47				7.43				9.44			
4.22				5.48				7.44				9.46			
4.23								<b>8 Production and In Process Controls</b>				<b>10 Storage and Distribution</b>			
4.24				<b>6 Documentation and Records</b>				8.1				10.1			
4.3				6.1				8.10				10.10			
4.30				6.10				8.11				10.11			
4.31				6.11				8.12				10.2			
4.32				6.12				8.13				10.20			
4.33				6.13				8.14				10.21			
4.34				6.14				8.16				10.23			
4.4				6.15				8.2				10.24			
4.40				6.17				8.20							
4.41				6.18											
4.42				6.2											
				6.20											

Audit Report

#### 4. General information

Give an overview of the company and site such as whether it is part of another group, how the company was formed, previous site names, what is the nature of the sites business and how many APIs or Intermediates are manufactured, site size

Give an overview of their inspection record and which health authorities have inspected the auditee

#### 5. Organisation and Personnel

Give an overview of the staffing levels for the site and departments plus working patterns.

Give an overview of the training system and the level and frequency of GMP training. Indicate if contract staff are used and if so for what operations and how they are trained.

#### 6. Quality Systems

Give an overview of the quality management system and practices of the site. Give an overview of the quality systems reviewed, including but not limited to change controls, deviation investigations and reporting, CAPA management, risk management applications, validation, recall systems, complaint management, internal audit programme

Give an overview Annual Product Review(s) reviewed and their compliance to ICH Q7 and conclusions.

#### 7. Facilities

Give an overview of the facilities visited and assessed. Indicate what utilities are used on the site and are under the responsibility of the site/or third party.

If necessary indicate the buildings and infrastructure ages and include main areas such as production buildings, solvent storage, warehousing and laboratory. If more than one API or facility is used for manufacture, indicate which ones are relevant to the product(s) being assessed.

Indicate if facilities are of suitable design and permit access to equipment for ease of cleaning and maintenance.

Indicate if the warehouse(s) are adequately monitored and controlled for temperature and relative humidity. Ensure facilities and utilities that need to be monitored are suitably

# DATA INTEGRITY

## AUDIT EXPERIENCES

- Access rights to GMP systems not available or not acceptable
- User-level are not defined (admin vs user)
- General accounts
- Storage of originals with effect onto document integrity
- Retest without reason
- Falsification of results
- No back-up system

# DATA INTEGRITY

## EXAMPLES: REQUIREMENTS FROM THE FDA GUIDANCE

- I. INTRODUCTION..... 1
- II. BACKGROUND ..... 1
- III. QUESTIONS AND ANSWERS..... 2
  - 1. Please clarify the following terms as they relate to CGMP records:..... 2
    - a. What is “data integrity”? ..... 2
    - b. What is “metadata”? ..... 3
    - c. What is an “audit trail”?..... 3
    - d. How does FDA use the terms “static” and “dynamic” as they relate to record formats? ..... 3
    - e. How does FDA use the term “backup” in § 211.68(b)?..... 4
    - f. What are the “systems” in “computer or related systems” in § 211.68?..... 4
  - 2. When is it permissible to exclude CGMP data from decision making?..... 4
  - 3. Does each workflow on our computer system need to be validated? ..... 4
  - 4. How should access to CGMP computer systems be restricted? ..... 5
  - 5. Why is FDA concerned with the use of shared login accounts for computer systems? ..... 6
  - 6. How should blank forms be controlled? ..... 6
  - 7. How often should audit trails be reviewed?..... 6
  - 8. Who should review audit trails? ..... 6
  - 9. Can electronic copies be used as accurate reproductions of paper or electronic records? ..... 7
  - 10. Is it acceptable to retain paper printouts or static records instead of original electronic records from stand-alone computerized laboratory instruments, such as an FT-IR instrument? . 7

- 11. Can electronic signatures be used instead of handwritten signatures for master production and control records?..... 8
- 12. When does electronic data become a CGMP record? ..... 8
- 13. Why has the FDA cited use of actual samples during “system suitability” or test, prep, or equilibration runs in warning letters? ..... 9
- 14. Is it acceptable to only save the final results from reprocessed laboratory chromatography? ..... 9
- 15. Can an internal tip regarding a quality issue, such as potential data falsification, be handled informally outside of the documented CGMP quality system? ..... 9
- 16. Should personnel be trained in detecting data integrity issues as part of a routine CGMP training program? ..... 10
- 17. Is the FDA investigator allowed to look at my electronic records? ..... 10
- 18. How does FDA recommend data integrity problems identified during inspections, in warning letters, or in other regulatory actions be addressed? ..... 10

# Registration

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