TOP 10

DEFICIENCIES

IN

New applications for Certificates of Suitability for chemical purity

1

Lack of manufacturing process details

- Deficient synthetic flow diagrams
- Inconsistencies in process descriptions
- Lack of raw material quantities

2 & 4

Inadequate specifications for intermediates and starting materials

- Lack of appropriate acceptance criteria for impurities
- Discrepancies in mass balance

3

Absence of potential mutagenic impurities discussion

- **Lack of reference to ICH M7 when listing and classifying impurities**
- **Deficient control strategy**

5

Inadequate raw material specifications

- Deficient specifications
- Missing impact of raw materials on impurity profile

6

Inadequate addressing of reprocessing and recovery

- **Lack of detailed description**
- **Absence of Clarity on reprocessing triggers**

7

Lack of Nitrosamines risk assessment

- **Appropriate Guidelines not used for building comprehensive risk assessment**
- **Absence of discussion of risks from materials and degradation**

8

Failure to address related substances

- Missing discussion beyond Ph. Eur. impurities
- Suitability of Ph.Eur. monograph to control in house impurities not addressed

9

Deficient discussion on residual solvents

- Missing LOD when “not detected” claims
- Lack of discussion for class 1 solvents

10

Inadequate starting material identification

- Requirements for acceptable starting materials not in line with ICH Q11 and Q&A
- Starting materials misidentified as reagents

Source document

European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

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