CleAnIng vAlidAtion of solutIon prOduCtIon in a hospItal phArMacy

N Ott, U LösCh, S Deuster

Hospital Pharmacy, University Hospital Basel, Spitalstrasse 26, CH-4031 Basel

Objectives

Hospital pharmacies often have a limited amount of technical equipment to produce a large portfolio of pharmaceutical products. Therefore, multipurpose equipment is used for manufacturing of different pharmaceutical preparations, introducing the risk of transferring contaminants to secondary products. Cleaning of technical equipment should remove residues of products and cleaning agents, as well as avoid microbial contamination, to guarantee patient safety and high quality of subsequent products [1]. Therefore, effective cleaning procedures should be developed and validated for all process equipment wetted by the product. Subsequently, the risk of contamination for all possible production lines of liquid manufacturing could be assessed.

Methods

1. Evaluation of critical equipment/surfaces (multipurpose equipment with product contact)

- 20 systems
- 11 non-critical
- 4 critical

Part of the cleaning validations
- 2 with cleaning validation
- 1 without cleaning validation

2. Evaluation of the cleaning procedures

- Use of residue-free cleaning agents (H₂O, EiOH)
- no cleaning validation for the cleaning agents
- no toxicological assessment for parenteral production necessary

3. Evaluation of the worst case active component

- 2 criteria: poorest water solubility (< 100 g/l) – physicochemical issue
- worst case for aqueous cleaning agents (H₂O, EiOH)
- lowest therapeutic dose – pharmacological issue
- worst case for permitted limits

Target: One worst case active component enables an assessment of all production lines
- evaluation of the whole available portfolio (32 products) ➔ Naphazoline nitrate

4. Analytical method validation of the worst case active component (HPLC)

Results

Equipment of non-sterile production: active component residue after cleaning

Addition of residues for the total solution production process

Discussion and Conclusions

- Residues of the active component may adhere to the inner surface of the tubes (PTFE).
- These residues are very difficult to remove by cleaning.
- After 24 hours, residues of the active component were dried, whereby removal of lipophilic active components with hydrophilic agents is more complicated.
- Turbulent flows and the rinsing of cavities from both directions could achieve a better cleaning outcome.
- A dried surface, consisting of stainless steel or PTFE, can reach the same microbiological results as an identical autoclaved material.
- PDE value: The maximum acceptable active component residue is referenced to the PDE value (permitted daily exposure), which reflects an accepted daily exposure of constant magnitude over a lifetime [1]. Patients’ stays in hospitals are usually short or medium term. Therefore the use of the PDE value as the acceptable limit of active component residue for production in hospital pharmacies is limited. The evaluation of the residue limits with PDE value should be conducted as a risk assessment, considering batch size, maximum daily dose and duration of therapy.

Acknowledgement

We would like to thank all members of the production, quality control and quality assurance units of the Hospital Pharmacy of the University Hospital Basel.

Literature:

Presentation:
23rd EMAP Congress
21–23 March 2018, Gothenburg (Sweden)

3PC-037

Corresponding author:
Norman Ott
University Hospital Basel, Spitalpharmazeut Scoliastrasse 26, CH-4031 Basel
norman.ott@usz.ch

Universitätsspital Basel