## 3PC-042 A SCIENCE- AND RISK-BASED STRATEGY TO QUALIFY STERILISED PREFILLED SYRINGES AS PRIMARY PACKAGING MATERIAL IN A HOSPITAL PHARMACY

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**Background** To improve medication safety in hospitals, The Joint Commission International standard recommend implementation of ready-to-administer (RTA) drugs. Many hospital pharmacies facilitate this in aseptic filling of polypropylene single-use syringes. The main disadvantages of this product, though the container is not meant for storage, are the aseptic process, the short shelf-life and the refrigerator capacity. The solution was found in a cyclic olefin polymer (COP) syringe, which can be terminally sterilised. All individual components of the syringe comply with the regulatory demands but to ensure that the new product does not adversely affect patient safety or product quality qualification is required.

**Purpose** A science- and risk-based strategy to qualify COP syringes as primary packaging material for the production of terminally sterilised RTA syringes with a high speed (semi-) automatic filling and closing machine in a hospital pharmacy.

**Material and methods** A 50 ml COP syringe with a polypropylene/butyl rubber tip cap and a butyl rubber stopper and a 5 ml COP syringe with an elastomer tip cap and a butyl rubber stopper were used for qualification. Validation batches of NaCl 0.9% with phosphate buffer pH 2, 5.8, 8 and 11, NaCl 0.9%, isopropyl alcohol (IPA) 5% in water and water for injections were produced. On t=0, 1, 2, 3, 4, 5, 6, 9, 12, 18 and 24 months the following tests were performed on the batches; clarity and degree of opalescence of the solution (Ph. Eur. 2.2.1.), degree of colouration of the solution (Ph. Eur. 2.2.2), pH of the solution, absorbance (Ph. Eur 3.2.2.1), reducing substances (Ph. Eur. 3.2.2.1), transparency (Ph. Eur 3.2.2.1), weight loss, subvisible particles (Ph. Eur. 2.9.19), silicon, closure integrity and sterility (Ph. Eur. 2.6.1).

**Results** All performed tests complied with acceptance criteria according to the Ph. Eur. Monographs. High pH value (11.8) showed higher absorbance, indicating more extractables and leachables; maximum 0.06 at t=24 months) than neutral pH ranges (5–8); and maximum 0.02.

**Conclusion** The syringes are suitable as primary packaging material for producing RTA products in a hospital pharmacy.

### REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

## 3PC-043 NEW FORMULATION OF NOREPINEPHRINE SOLUTION IN PREFILLED CYCLIC OLEFIN STERILISED SYRINGES

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**Background** Norepinephrine is a potent α-sympathomimetic drug which plays an important role in the acute treatment of hypotension and shock in an intensive care unit. Commercially available norepinephrine solutions contain sodium metabisulfite ($Na_2S_2O_5$) as an antioxidant. However, the cyclic olefin polymer syringe used in our hospital is not compatible with sodium metabisulfite due to brown colourisation of the syringe during sterilisation.

**Purpose** To develop a new formulation of 0.1 mg/ml norepinephrine solution without sodium metabisulfite which is chemically stable and sterile.

**Material and methods** Pre-formulation tests were performed with 0.1 mg/ml norepinephrine solution with 0, 0.05% and 0.1% ascorbic acid added as an antioxidant. Other excipients were 0.1 mg/ml edetate sodium, 8 mg/ml sodium chloride and water for injections. The syringes were filled under nitrogen gassing, stored at room temperature and protected from daylight. Concentration of norepinephrine was measured at day 0, 8, 21 and 51, and 3 and 5 months with an UHPLC system with diode array detection. Based on the pre-formulation test results, the final formulation was defined and stability testing was performed measuring concentration of norepinephrine, pH, clarity, colour of solution, subvisible particles and sterility at time intervals according to ICH guidelines.

**Results** The norepinephrine concentration in the pre-formulation tests were 98.4%, 96.4% and 96.4% at t=5 months for, respectively, no ascorbic acid added, and 0.10% and 0.05% ascorbic acid added. Validation batches were produced with norepinephrine, edetate sodium, sodium chloride and water for injections filled under nitrogen gassing. Preliminary results show a concentration of 108.8% and 109.0% norepinephrine (10% more norepinephrine was added due to possible degradation during sterilisation based on historical data) at t=3 months.

**Conclusion** Norepinephrine (0.1 mg/ml) solution without sodium metabisulfite in a sterilised syringe stored at room temperature protected from daylight, is stable for at least 3 months.

### REFERENCE AND/OR ACKNOWLEDGEMENTS

Larmené-Beld K, Kuiper A, van Berkel S, et al. *A science- and risk-based strategy to qualify sterilised prefilled syringes as primary packaging material in a hospital pharmacy.* Abstract submitted for 24th EAHP Congress 2019.

No conflict of interest.

## 3PC-044 PARAFFIN OIL-BASED EMULSION: INFLUENCE OF GUM ARABIC AND THE MIXING RATE ON EMULSION STABILITY

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**Background** Emulsions form the basis of a wide range of manufactured products in the pharmaceutical domain. They are constituted by at least two non-miscible liquids. However, instability is the major inconvenience of these galenic forms.

**Purpose** Paraffin oil and gum arabic are used in the formulation of the oil-in-water emulsion type, which has a lot of applications in drug delivery, either as a medicament or as a vehicle. In the hospital pharmacy, the emulsion for intravenous