observed in particle size after 60 days in all samples. The organoleptic characteristics (smell, taste and texture) remained unchanged in all of the preparations until the third month.

**Conclusion and relevance**
A stable alcohol free diazepam suspension was achieved. The tablets produced a more stable formulation than the bulk source, especially when stored at a lower temperature. This formulation can solve the problem of shortages, allowing the appropriate administration of paediatric treatments, while allowing compliance with the recommended composition limits of ethanol, by excluding this excipient from its composition.

**REFERENCES AND/OR ACKNOWLEDGEMENTS**
No conflict of interest.

### 3PC-029
**PAEDIATRIC DRUG RESISTANT EPILEPSY: NITRAZEPAM 1 MG/mL SOLUTIONS TO AVOID CLINICAL THERAPEUTIC ERROR**

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Background and importance: The management of paediatric patient with drug resistant epilepsy (EDR) is complicated and often requires therapy and dose adjustments. The clinical pharmacist and child neuropsychiatry unit cooperate to prevent clinical therapeutic errors, common in the prescription of drugs with reduced and personalised dosages.

Nitrazepam (NTR) in children is recommended in epileptic spasms, in Dravet, West and Lennox–Gastaut syndromes. There is a probable risk of administration error due to the low prescribed dosage (125 µg/kg) and crushing of commercial tablets.

**Aim and objectives**
To make a liquid formulation with a standard concentration, easily adaptable to paediatric needs as weight changes, that is palatability, suitable and simple to use during hospitalisation and at home.

**Material and methods**
Multiphase study:
- **Phase I:** data collection.
  - Retrospective study examined the medical records of children born 2008–2019 with a certain diagnosis of EDR: patient number, sex, age, epilepsy classification according to the International League Against Epilepsy criteria, antiepileptic therapy and dose of drug were collected.
- **Phase II:** subject study of nitrazepam, its dosage and the galenic compounding formulation it was possible to use.
- **Phase III:** chemical–physical–microbiological stability analysis of nitrazepam 1 mg/mL.

Samples were stored for 30 days at 2–8°C and/or ambient at 25°C. Chemical–physical stability was measured by quantitative determination of the molecular ions of nitrazepam C282.1/C236, using high pressure liquid chromatography (HPLC), equipped with a UV detector, interfaced with a triple quadrupole mass detector (mass spectrometer, MS/MS), column Luna C1850 mm, standard nitrazepam DS 100 µg/mL. Microbiological stability was assessed according to the Italian Ufficiale Farmacopea (FUI).

**Results**
A total of 101 children with EDR (54 males, 47 females) were studied, aged mainly 3–4 years (20%) and 9–10 years (33%). Classifications: focal onset in 34.86%, focal to bilateral tonic–clonic in 17.10%, generalised onset in 47.36% and unclassified in 0.65%. Thirty-one drugs are prescribed, the most used were: levetiracetam (27%), clobazam (25%), topiramate (21%) and NTR (12%). Required dosages of NTR difficult to administer: 0.625 mg, 0.83 mg, 1.25 mg, 1.66 mg and 2.5 mg. Three liquid galenic formulations were set up (NTR from Mogadon 5 mg tablets): NTR 1 mg/mL simple syrup methylcellulose 1%, NTR 1 mg/mL suspension tragacanth gum and NTR 1 mg/mL Sysrend SF AlkaDry.

HPLC MS/MS analysis confirmed uniform and steady dosage, and 30 day stability for NTR 1 mg/mL suspension and NTR 1 mg/mL Sysrend SF AlkaDry.

**Conclusion and relevance**
Good clinical practice and collaboration between departments allowed better management of epileptic seizures in children affected by severe EDR. Reproducible and safe therapy means improving patient’s life and therapeutic compliance.

**REFERENCES AND/OR ACKNOWLEDGEMENTS**
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No conflict of interest.

### 3PC-030
**ANALYTICAL METHOD VALIDATION TO CARRY OUT PHYSICOCHEMICAL STABILITY STUDIES OF METHADONE ORAL SOLUTIONS**


Background and importance: On the basis of resolution 189/2018 published by our city health council, the hospital pharmacy service was entrusted with the centralisation of the procedure for the acquisition, compounding, distribution and dispensing of methadone to drug addicts in integral attention centres. In order to improve and increase the beyond use date (BUD) of methadone oral solutions, we carried out a physicochemical stability study.

**Aim and objectives**
To develop an analytical method and validation to carry out a physicochemical stability study of two oral solutions of methadone to increase their BUD. Method development should be made in an effective and reproducible manner.

**Material and methods**
The study was carried out on two formulations of methadone 10 mg/mL, which were prepared with and without parabens as preservatives. A high performance liquid chromatography (HPLC) Agilent 1100 was used, provided with a quaternary pump and an ultraviolet diode array detector to determine methadone. First we carried out the analytical method development to achieve the analytical performance characteristics. Then we performed validation of the analytical method obtaining linearity, instrumental intra-assay and inter-assay precision, and accuracy and recovery percentage.

**Results**
Chromatographic conditions were: flow rate 1.6 mL/min, 55% acetonitrile and 45% phosphate buffer (adjusted to pH=10) as the mobile phase. Injection volume was 50 µL,
the temperature in the column compartment was 40°C. The column used was the Xterra C18 because methadone pKa is 8.3. Retention time for methadone was 4.5 min and for parabens 1.5 min.

The final methadone determination method was validated for a standard of 10 mg/mL and applied for the determination of methadone with two parabens. The most relevant results were: correlation coefficient r=0.9957 for methadone in the range tested (7.5–12.5 mg/mL); instrumental precision 0.33% for standards (n=10); intra-assay precision 0.53% (n=6) and inter-assay precision 1.95% (n=12). The relative standard deviation percentage for accuracy was 1.28%, and the percentage recovery was 101.5 ±1.5%.

Conclusion and relevance Analytical method development and validation procedures are vital in the discovery and development of drugs and pharmaceuticals to ensure performance of the method. The proposed HPLC conditions to determine methadone were proved to be valid and reproducible for carrying out physicochemical stability studies of different methadone oral solutions.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

3PC-032 AUTOLOGOUS TISSUE ADHESIVE IN OPHTHALMIC SURGERY

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Background and importance Sutures to replace tissue adhesives have enhanced importance. However, commercialised drugs are allogenic, synthetic and expensive, increasing surgery costs.

Aim and objectives
1. To produce an autologous tissue adhesive (ATA) easily compounded in ophthalmological surgery.
2. To show evidences of the safe and effectiveness of the ATA in preclinical studies.

Material and methods To produce 4 mL of ATA based on a fibrinogen (FC) and thrombin concentrate (TC) (proportion 1:1), 20 mL of donor blood plasma were precipitated with protamine to prepare FC, and then 20 mL of plasma were precipitated with acetic acid to obtain a TC in a buffer (CaCl₂, NaHCO₃, NaCl). Drug was conditioned in two 2 mL syringes for topical ophthalmic administration by mixing with a needle.

The in vitro toxicity of the drug was studied in a human corneal epithelial model (described as QobuR), to evaluate the grade of irritation after 30 min of exposition time.1

Pterygium surgery was performed in four eyes of white New Zealand rabbits, using ATA to fix a frontal conjunctival autograft (4×5 mm) into the temporal bulbar conjunctive.

The grafted eyes were evaluated in vivo by clinical evaluation for 14–28 days and ex vivo by histology.

Results ATA produced from each donor showed a mean of 18.0 g/L of fibrinogen and 1500 UI/mL of thrombin. ATA instantly produced homogeneous clots when it was mixed with a needle.

Three in vitro studies of four ATA showed non-irritation due to high survival cell viabilities (>80%).

Good preclinical results were found:
- 20 mm² autograft could be fixed successfully.