was validated according to the International Conference on Harmonisation Q2 (R1). Four syringes for each condition were prepared. Physical stability was evaluated by visual and subvisual inspection (turbidimetry by UV spectrophotometry at 350, 410 and 550 nm).

Results For each solvent, solutions at 125 mg/mL retained more than 90% of the initial concentration for 24 hours: for 0.9% NaCl (minimum $96.57\% \pm 1.69\%$; maximum $95.96\% \pm 1.38\%$) and for D5W ($94.96\% \pm 1.38\%$; $98.08\% \pm 0.48\%$). After 48 hours of storage, the solutions contained <90% of cloxacillin: a minimum of $89.58\% \pm 0.43\%$ for 0.9% NaCl and $89.47\% \pm 0.79\%$ for D5W. During the study, pH values decreased progressively during the 48 hours of storage and pH differences were >1 pH unit after 48 hours for both solvents. During the subvisual examination, absorbance values at 410 and 550 nm increased after 48 hours. A colour change was observed at 48 hours (from colourless to very slight yellow) in 0.9% NaCl. In D5W, the solutions stained more quickly; a very slight yellow colouration was visible after 6 hours of storage which intensified after 24 and 48 hours.

Conclusion and relevance Cloxacillin solutions at 125 mg/mL in 0.9% NaCl and D5W were stable in polypropylene syringes for 24 hours at room temperature. The solutions were unstable after 48 hours of storage.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of interest No conflict of interest

3PC-062

IMPACT OF THE PREPARATION OF 1.0 MG/ML NIVOLUMAB CLINICAL SOLUTION ON THE PARTICULATES (AGGREGATION) MEASURED BY DYNAMIC LIGHT SCATTERING: NaCl AND GLUCOSE CONCENTRATION AND AGITATION EFFECT

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Background and importance Nivolumab (Opdivo) is a human immunoglobulin G4 monoclonal antibody that binds to programmed death receptor 1 (PD-1) and blocks its interaction with PD-L1 and PD-L2. As a complex protein, routine handling or unintentional mishandling of its solutions may cause degradation that could remain unnoticed but could potentially compromise the clinical safety and efficacy of the drug product.¹

Aim and objectives To assess the impact on the nivolumab (Opdivo) aggregation process promoted by slight modification in the concentration of the compound (NaCl 0.9% or glucose 5%) used to prepare the clinical diluted solution of nivolumab at 1.0 mg/mL. Also, to assess the impact on the aggregation on nivolumab clinical diluted solutions (1.0 mg/mL, in NaCl 0.9% and glucose 5%) promoted by agitation stress.

Material and methods Nivolumab (Opdivo, 10 mg/mL) was diluted at 1 mg/mL using different NaCl (from 0.5% to 1.5%) and glucose (from 1% to 10%) solution concentrations. Also, clinical diluted solutions were subjected to manual gentle agitation (for 30 s and 1 min) and vortex agitation (Vortex VibraMix, 3000 rpm for 10 s, 30 s and 1 min). Particulate

was tracked by dynamic light scattering (DLS) using a Malvern Zetasizer Nano ZS90.

Results Reference samples of diluted nivolumab at 1.0 mg/mL in NaCl 0.9% and 5% glucose showed a single particulate population with a hydrodynamic diameter (HD) of 9.66 ± 2.96 nm and 10.67 ± 2.68 nm, respectively, attributed to nivolumab monomers. No significant changes were obtained for HD when the concentration of the diluents was changed. Also, no significant changes were observed after performing the agitation stresses, showing that the HR values were always in the interval of the size of the monomers.

Conclusion and relevance Variation in NaCl and glucose concentrations around the clinical concentrations of 0.9% and 5% did not promote aggregation in a 1 mg/mL nivolumab solution detected by DLS. Also, agitation did not have any impact on aggregation on this clinical nivolumab solution.

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3PC-063

PERFORMANCE QUALIFICATION OF ROBOTIC SYSTEM FOR CYTOTOXIC DRUG PREPARATION IN A FULLY GMP COMPLIANT HOSPITAL PHARMACY

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Background and importance A robotic system for automated preparation of cytotoxic drugs, such as APOTECACHemo, ensures reduced occupational exposure to toxic substances and aseptic conditions. The most critical operations are performed by a robotic arm; the operator's intervention is limited to loading/unloading materials in a rotating warehouse through an unloading/loading area enclosed within a laminar airflow barrier. In European hospital pharmacies which comply with good manufacturing practice (GMP), the performances of the robot are assessed by GMP qualification to confirm that the technology meets the set quality standards.

Aim and objectives The aim of this study was to evaluate microbiological performances and environmental conditions during fully automated preparation with APOTECACHemo in a grade B cleanroom.

Material and methods Effectiveness of laminar airflow retention was checked by potassium iodide (KI) discus test in the unloading/loading area of the APOTECACHemo robot. Aseptic preparation of cytotoxic drugs was evaluated with media fill simulation tests on three consecutive days. In total, 240 products (180 infusion bags, 30 syringes, 30 elastomeric pumps) were automatically filled with single/double strength tryptic soy broth in lieu of drug products. Microbiological environmental controls were performed by passive air sampling (settle plates, four locations), surface sampling (contact plates/swabs, 14 locations), and active air sampling (three locations). Samples were taken for each shift. Media fill products were