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%±1.69%; maximum 95.96% ±1.38%) and for D5W (94.96%±1.38%; 98.08%±0.48%). After 48 hours of storage, the solutions contained <90% of cloxacillin: a minimum of 89.58%±0.43% for 0.9% NaCl and 89.47%±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

visually inspected for turbidity after 14 days of incubation. The number of colony forming units (CFU) per plate were counted and identified.
Results The results of the KI discus test were far below the acceptance limit, demonstrating the effectiveness of laminar airflow in preventing the escape of particles from the internal areas of the robot. None of 240 media fills showed turbidity after incubation, thereby indicating no contamination with microorganisms. The working area met the grade A limit (0 CFU/sample). In the warehouse, 1 CFU was found in two samples (mean 0.2 CFU/contact plate, 0.1 CFU/settle plate). Microbial contamination was slightly higher in the loading area (mean 0.3 CFU/contact plate, 0.8 CFU/settle plate). Most of the CFUs were identified as skin related microorganisms, such as *Staphylococcus epidermidis* and *Staphylococcus hominis*.
Conclusion and relevance Extensive media fill tests and environmental monitoring during automated preparation with the robot revealed well controlled aseptic procedures and adequate sterility levels, thereby complying with the quality standard set by the hospital pharmacy.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of interest No conflict of interest

3PC-064 A MULTICENTRE STUDY COMPARING CHEMOTHERAPY PREPARATIONS USING DIGITAL VIDEO MONITORING

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Background and importance Preparation of chemotherapy treatment is a risky step. Therefore, the production circuit in the chemotherapy reconstitution unit (CRU) must be secured. The Drugcam digital tool is a preparation control system that guides the hospital pharmacy preparer (HPP) in their manufacturing process.
Aim and objectives A remote, multicentre and retrospective digital audit analysed qualitatively and quantitatively the practices of different CRU to find ways to optimise the preparation step for chemotherapy treatment.
Material and methods Over 1 year, data from 10 public and private healthcare institutions on three types of chemotherapy treatment, lyophilisate (pemetrexed), ready-to-use standard dose (nivolumab 240 mg) and dispenser (5-fluorouracil (5-FU)) were collected. This study analysed quantitative data extracted in Excel by pharmacists using local Drugcam data. Qualitative data obtained from audits made by pharmacists analysing 10 video recordings per chemotherapy preparation were also analysed.
Results 14 218 preparations made by 119 HPP were analysed: 2217 pemetrexed by 99 HPP, 1819 nivolumab by 90 HPP and 12827 5-FU by 110 HPP. The median preparation times for pemetrexed, nivolumab and 5-FU from all centres were 6.2, 4.2 and 4.9 min, respectively. Regardless of the three molecules, the results showed no significant difference between the experience of the Drugcam preparer and its productivity.

Qualitatively, analysis of the films showed heterogeneous practices between establishments: no compress for all stages, reconstitution by shaking of the lyophilisate as well as its mirage was not protocoled and rapid injections into the solvent were observed. The equipment used (infusion line or extension for infusion tree), the Drugcam practice (labelling of the preparation filmed or not, automatic or not automatic detection by the data matrix of the solvent/vial bags) and the organisation of each centre had a strong impact on the quality and productivity of the centres.
Conclusion and relevance If this study showed no correlation between time production, annual number of preparations and number of HPP, the analysis will allow us to recommend the practices of Drugcam for the preparation of chemotherapy treatment. Moreover, organisational modifications (series preparation, change of material reference) and practice harmonisation (standardised reconstitution of lyophilisates) will improve productivity and safety.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of interest No conflict of interest

3PC-065 IMPACT OF LIGHT STRESS ON THE ISOFORM PROFILE OF NIVOLUMAB (OPDIVO) IN OPENED VIALS ESTIMATED BY (RP)UHPLC-UV-(HESI/ORBITRAP)-MS

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Background and importance Nivolumab (Opdivo) is a human IgG4 monoclonal antibody from the group of immunomodulators which bind to the programmed death receptor 1 (PD-1). As a complex protein, physical aggregation and chemical degradation can occur throughout its life, and even modest environmental stresses can cause extensive damage.[1] As indicated in its technical report,[2] the unopened vials can be stored at a controlled room temperature up to 25°C with room light for up to 48 hours.
Aim and objectives To assess the impact on the isoform profile of nivolumab 10 mg/mL (Opdivo) promoted by exposure to light in its own opened vial at a controlled temperature of 25°C to evaluate likely risks from unintentional mishandling in real hospital conditions.
Material and methods Nivolumab (Opdivo, 10 mg/mL) was placed in an accelerated stress test chamber to simulate sunlight (Solarbox 3000e RH, Cofomegra, Milan, Italy) for 24 hours at 25°C. Irradiation was set at 250 W/m^2, between 320 and 800 nm.[3] A validated reverse phase ultra high resolution liquid chromatography coupled to high resolution mass spectrometry and exact mass ((RP)UHPLC-UV-(HESI/Orbitrap)-MS) method was used to analyse intact nivolumab. UV-chromatograms and total ion chromatograms (TICs) were recorded and the deconvoluted mass spectra gave the nivolumab mass isoform profile.
Results UV chromatograms and TICs suggested no degradation products after light exposure. However, isoform profiles clearly showed changes in the light submitted nivolumab