pH of 5.4. There are no published data to support how pH affects mitomycin C stability in 0.9% sodium chloride solutions (NSS).

Aim and objectives To study the stability of mitomycin C in NSS under different pH conditions and storage temperatures.

Material and methods A stability study was carried out in eight NSS with a commonly used mitomycin C concentration of 0.12 mg/mL. Solutions were prepared in duplicate for each pH: 4.5, 5.5, 6 and 7. The pH was adjusted with sodium hydroxide or phosphoric acid. Four solutions were stored at room temperature and four at 5°C. Mitomycin C concentration was assessed at 0, 30, 60, 120 and 300 min and 24 hours by high performance liquid chromatography. The areas obtained were compared with the initial area (time 0 min) to calculate the remaining mitomycin C percentage. A 10% level of degradation is assumed as the limit in terms of stability.

Results Remaining mitomycin C percentages were calculated. Analysing the results at room temperature, the remaining mitomycin C percentages were 98.5% at 30 min; 97.2% at 60 min; 92.7% at 120 min; 89.3% at 300 min; and 88.4% at 1 hour at pH=7. Remaining percentages were 99.2%, 98.6%, 97.6%, 95.8% and 87.4%, respectively, at pH=6. Percentages were 98.9%, 98.2%, 96.6%, 93.5% and 87.3%, respectively, at pH=5.5. Percentages for pH=4.5 were 98.0%, 96.7%, 88.1%, 85.4% and 83.2%, respectively. The concentration of all solutions remained above 90% of the initial concentration after 1 hour, regardless of the pH value, in contrast with the values at 24 hours.

Analysing the concentrations at 5°C, the remaining mitomycin C percentages were 99.2%, 98.4%, 97.3%, 94.9% and 90.0% at pH=7. Remaining percentages were 99.5%, 99.2%, 98.6%, 97.4% and 94.0%, respectively, at pH=6. Percentages were 99.8%, 99.6%, 99.2%, 98.4% and 95.3%, respectively, at pH=5.5. Percentages for pH=4.5 were 99.8%, 99.7%, 99.3%, 98.5% and 93.1%, respectively, for each time studied. All solutions stored in the fridge were stable over the 24 hours of the study.

Conclusion and relevance We demonstrated that the stability of mitomycin C solutions decreased over time and with lower pH values in NSS. Furthermore, room temperature significantly affected mitomycin C stability. However, degradation was greatly reduced at 5°C, regardless of pH. This proves that mitomycin C solutions in NSS can be stored in the fridge for 24 hours.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

3PC-019 IN USE PHYSICOCHEMICAL AND MICROBIOLOGICAL STABILITY OF DILUTED SOLUTIONS OF THE MONOCLONAL ANTIBODY NIVOLUMAB

¹M Rivano*, ²F Selmin, ¹L Camuffo, ¹L Cancanelli, ¹G Mangoni, ¹MA Piccoli, ³G Longobardo, ²F Cilurzo, ²P Minghetti. ¹University of Milan, School of Hospital Pharmacy, Milan, Italy; ²University of Milan, Department of Pharmaceutical Sciences, Milan, Italy; ³Ircs San Raffaele, Pharmacy, Milan, Italy

10.1136/ejhp-pharm-2020-eahpconf.66

Background and importance Nivolumab, a fully human IgG4 anti-PD-1 monoclonal antibody, is available as a concentrated solution for intravenous (IV) injection and diluted in 0.9% saline. These solutions are reported to be physically and chemically stable for 24 hours at 2–8°C and a maximum of 8

hours at 20–25°C. As the ‘real world’ use after dilution in IV infusion bags may exceed the manufacturer’s recommendations, ‘in use’ studies assessing their stability is important as the formulation components are diluted and may not be able to protect the protein against degradation or denaturation.

Aim and objectives The aim of the study was to assess physicochemical and microbiological in use stability of diluted solutions of nivolumab stored at 2–8°C.

Material and methods Four polyolefin bags of nivolumab were compounded under aseptic conditions at a concentration of 2 mg/mL with 0.9% saline solution and stored at 2–8°C over a 7 day period. At selected time points, different methods were used to evaluate stability: pH, osmolality, turbidimetry, dynamic light scattering (DLS), size exclusion chromatography-high performance liquid chromatography (SEC-HPLC) and gel electrophoresis. Microbiological assays were also performed after 30 days.

Results Diluted nivolumab solutions remained clear and colourless with no visible particles during the test period. Physicochemical analyses demonstrated that all samples were not affected in terms of formation of subvisible particles or changes in pH or osmolality. Results of SEC-HPLC analyses revealed no change in high molecular weight, soluble aggregate or low molecular weight fragmented product. Moreover, the relative ratio remained constant over time. These results were also confirmed by gel electrophoresis under both non-reducing and reducing conditions as no change in band distribution was detected. Finally, no bacterial or fungal contamination was observed in any of the samples tested after 30 days of storage.

Conclusion and relevance These analyses demonstrated that nivolumab under the dilution conditions required for IV infusion can be stored for 7 days at 2–8°C with no evidence of physical or chemical alteration. When further data are available on how quality and potency may vary over time under different environmental factors, these results may support the possibility of compounding ‘dose banding’ batches in order to improve the patient’s management, pharmacy workload and reduce costs.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

3PC-020 PHYSICOCHEMICAL STABILITY OF 25 MG/ML PEMETREXED DIARGININE IN PARTIALLY USED VIALS AND 3 AND 12 MG/ML DILUTED IN DEXTROSE 5% IN POLYOLEFIN BAG

YE Nisse*, J Vigneron, N Sobalak, B Demoré. Chru Nancy, Pharmacy, Vandoeuvre-Lès-Nancy, France

10.1136/ejhp-pharm-2020-eahpconf.67

Background and importance A new pemetrexed salt, pemetrexed diarginine (PDA), was recently marketed by Mylan. The product is a ready to dilute 25 mg/mL solution. The manufacturer indicates 24 hour stability after dilution in dextrose 5% (D5W).

Aim and objectives To study the stability of: (1) PDA in D5W polyolefin bag at 3 and 12 mg/mL protected from light (PFL) at 2–8°C and at 25°C; (2) PDA vial at 25 mg/mL partially used and perforated with a plastic spike PFL at 2–8°C and at 25°C; (3) PDA in D5W polyolefin bag at 3 and 12 mg/mL, not PFL at room temperature; (4) PDA vial at 25 mg/mL

partially used and perforated with a plastic spike, not PFL at room temperature.

Material and methods The stability study was performed by high performance liquid chromatography coupled to a photodiode array detector. The method was validated according to the International Conference on Harmonisation guideline Q2 (R1). Physical stability was evaluated by visual and subvisual inspection. pH values were measured.

Results PDA solutions PFL in D5W at 3 and 12 mg/mL retained more than 95% of the initial concentration after 7 days at 25°C and after 28 days at 2–8°C. PDA ready to dilute 25 mg/mL solutions PFL retained >95% of the initial concentration after 28 days at 25°C and 2–8°C. PDA solutions in D5W at 3 mg/mL and 12 mg/mL and PDA ready to dilute 25 mg/mL solutions not PFL retained >95% of the initial concentration after 7 days at room temperature. All samples had a pH in the range 8.05–8.77. A very light colouration, described in summary of product characteristics, to a more intense yellow–brown colouration, appeared depending on concentration and time. No precipitate was observed.

Conclusion and relevance According to the manufacturer's specifications (colourless to slightly brown–yellow) and to the chemical stability, defined as >95% of the initial concentration, PDA solutions in D5W at 3 and 12 mg/mL and PDA ready to dilute 25 mg/mL solutions PFL were stable for 7 days at 25°C and for 28 days at 2–8°C. PDA solutions in D5W at 3 and 12 mg/mL and PDA ready to dilute 25 mg/mL solutions not PFL were stable for 7 days at room temperature.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

3PC-021

STORAGE OF NIVOLUMAB PEMBROLIZUMAB AND DARATUMUMAB FOR 14 DAYS AFTER COMPOUNDING IN THE HOSPITAL PHARMACY: A MICROBIOLOGICAL STABILITY STUDY

L Cancanelli*, F Selmin, L Camuffo, G Mangoni, M Piccoli, M Rivano, F Cilurzo, P Minghetti. Università Degli Studi Di Milano, Department of Pharmaceutical Sciences, Milan, Italy

10.1136/ejhp-2020-eahpconf.68

Background and importance Viable microorganisms and/or endotoxins administered parenterally via contaminated preparations may lead to nosocomial infections, SIRS/sepsis and increased mortality of patients. The pharmacist has the responsibility to ensure that the product is stable in the final administered preparation.

Aim and objectives To verify if monoclonal antibodies such as nivolumab, pembrolizumab and daratumumab are promoters or inhibitors of microbial growth. Moreover, the microbiological stability of dilutions at clinically relevant concentrations were verified over a 14 day period.

Material and methods Samples, reconstituted according to the summary of product characteristics (SPC) in 1 mL syringes, were injected into standardised suspensions of *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Candida albicans*.¹ At different time points (ie, 0, 1, 3, 5, 24, 48 and 144 hours) an aliquot of 0.01 mL, containing about 100 CFU, was transferred to the trypticase soy agar plate and sabouraud dextrose agar+chloramphenicol plate. After 24 hours of incubation at

37°C, samples were assayed. Moreover, a total of 24 syringes were stored for 1, 3, 6, 7, 10 and 14 days before being incubated to determine microbiological stability according to the EP method.

Results The results showed that 144 hours after inoculation no colony forming units were detected for *the C albicans* and *S aureus* strains. The only microorganism that survived after 5 days was *P aeruginosa*. Comparing the control with the samples analysed, no significant growth or reduction in microorganisms were observed. The samples were all clear after 14 days of incubation.

Conclusion and relevance Compared with the control, no significant growth or reduction in microorganisms were observed, indicating that the monoclonal antibodies investigated cannot be used by the strains as substrates for their survival. It can also be deduced that these monoclonal antibodies have no bactericidal or bacteriostatic actions. Under these conditions, the monoclonal antibodies were microbiologically stable for 14 days. In conclusion, when data on 'in use' stability' are available for a period of 14 days, a new model of patient management in the day hospital and drug preparation in the hospital pharmacy could be organised.

REFERENCES AND/OR ACKNOWLEDGEMENTS

1. Sarakbi I, Federici M, Krämer I. Viability of microorganisms in novel chemical and biopharmaceutical anticancer drug solutions. *EJPPS* 2015;20:5–12.

No conflict of interest.

3PC-022

PARTICULATE QUALITY OF A CONTROLLED ATMOSPHERE AREA. COMPLIANCE WITH GOOD MANUFACTURING PRACTICES AT REST AND DURING ACTIVITY, HIGHLIGHTING FACTORS IMPACTING ON CONTAMINATION

M Pottier*, M Naveau, A Villain, G Strobbe, I Sakji, F Feutry, G Marliot. Centre Oscar Lambret, Pharmacy, Lille, France

10.1136/ejhp-2020-eahpconf.69

Background and importance The activity of chemotherapy preparations is constantly evolving:

1. It is increasing (+17% in our centre in 5 years).
2. Particulate quality monitoring is recommended but rarely done in hospital pharmacies.

The pharmacist, who is responsible for this activity, must anticipate these changes.

Aim and objectives We first demonstrated the compliance of our controlled atmosphere area with the ISO 7 (at rest) and ISO 8 (during activity) criteria. Then we determined the factors significantly impacting on the particle rate in order to design a mathematical model that would predict the number of particles and thus better control the increase in activity.

Material and methods The particle count was carried out according to the requirements of the ISO 7 and ISO 8 standards (particle size, sampling plan, volume, duration and height). We systematically recorded the following factors: date, time, number of people present in the controlled area, temperature, pressure, sampling location, sampling conditions (at rest or during activity) and equipment entering the ZAC mechanically cleaned or not. For the statistical analysis, a grouping of sampling points by critical sector (personnel entry