and 95.9% respectively, representing a reduction of 4.1% to 8.9%.

Conclusion and Relevance As expected, EGF concentrations decrease after filtration, especially when the porosity of the filter used is low. Moreover, the significance threshold is reached for P3 under SF. We may suppose that smaller AMs (ie IGF-1, MM 7.6 kDa; TGF-β1, MM 25 kDa) will be less retained. For larger AMs such as fibronectin (MM around 450kDa), the decrease in concentration is likely to have an impact on the ASEDs efficacy, justifying a more specific study. Other methods of ensuring the microbiological safety of ASEDs should probably also be considered.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest.

3PC-039 EARLY DE-RISKING OF THE STABILITY OF A PERSONALISED, STERILE BACTERIOPHAGE SUSPENSION ON THE BASIS OF ADVANCED KINETIC MODELLING

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Background and Importance Bacteriophages, natural viruses of bacteria, are a promising therapy against multidrug-resistant bacteria. The use of therapeutic bacteriophages (TBP) requires the selection of the most active ones and their individual formulations (hospital or magistral preparations) by a hospital pharmacy for a personalised medicine. The risk of TBP instability must be managed at the earliest stages of development.

Aim and Objectives Advanced Kinetic Modelling reliability assessment to de-risk the instability of BPT formulations.

Material and Methods A purified anti-staphylococcal BP (*Silviavirus*) formulated in two solutions (A and B) was tested. The main critical quality attribute to assess their stability was the biological activity, determined by numeration of Plaque Forming Unit (PFU) (Spot Test), with a target set at $(10 \pm 9).10^8$ PFU/mL. The following study designs were performed: (i) an accelerated degradation with seven temperature conditions (from -80 °C to +50 °C) during 3 months (analysis at D0, D7, D14, D28, D60, and D90), the data generated being used for AKM with PREDISTAB method; (ii) a prospective stability study based on spot test performed (n=3) at 5 and 25 °C during 12 months for A and 6 months for B.

Results The results (expressed in PFU/mL) of the prospective vs predicted stability studies were as follows:

- for solution A
- ^{8} vs $2.43x10^8$ (D_{LOG}=0.66%) and $1.04x10^5$ vs $2.65x10^5$ (D_{LOG}=8.1%)
- ^{8} vs $1.46\ x10^8$ (D_{LOG}=2.05%) and $3.56x10^2$ vs $4.76x10^2$ (D_{LOG}=4.94%)
- for solution B at 5° and 25°C after 6 months: $2.56x10^8$ vs $5.60x10^8$ (D_{LOG}=4.04%) and $1.67x10^4$ vs $2.69x10^3$(D_{LOG}=18.78%)

Conclusion and Relevance Our data suggest that AKM allows rapid assessment of the risk of instability for both formulations. Comparison of the results of the predictive vs prospective stability studies showed a good precision at 5 °C and 25 °C during 12 months for formulation A and 6 months for formulation B. The prospective study is still ongoing for both formulations to be compared with predictions at 24 months. The PREDISTAB method by identifying the risk of instability at the earliest stage of development should allow the early selection of the best TBP formulation and predict the expiry date.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest.

3PC-040 RADIOCHEMICAL PURITY DETERMINATION OF 177LU-PSMA-617: DEVELOPMENT AND VALIDATION OF A HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY ANALYTICAL METHOD

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Background and Importance ^{177}Lu-PSMA-617 is a treatment of progressive, metastatic, castration-resistant prostate cancers expressing PSMA receptors, previously treated with taxane and at least one second-generation hormone therapy. ^{177}Lu-PSMA-617 is a radiopharmaceutical drug with a marketing authorisation and is manufactured industrially (PLUVICTO®, Novartis). However, it can also be prepared in-house, especially for preclinical applications. Thus, quality control procedures are required to determine radiochemical purity (RCP).

Aim and Objectives To develop and validate a radio-high-performance liquid chromatography (HPLC) analysis method to measure RCP of ^{177}Lu-PSMA-617.

Material and Methods Radio-HPLC analyses were carried out on an apparatus equipped with a C_{18} column and a radioactivity detector. Three commercial ^{177}Lu-PSMA-617 batches were used as samples. The parameters considered for method validation were specificity, linearity, accuracy, precision, robustness, limits of detection (LOD) and limits of quantification (LOQ). Means, standard deviations and coefficient of variation (CV) for RCP, retention time (tr) and recovery were calculated. Linear regression coefficient R^2 was computed for linearity.

Results Radiochemical identification of ^{177}Lu-PSMA-617 consisted in 10 analyses of each three commercial batches and showed a consistent tr of 10.07 min (CV% < 0.1). Recovery was excellent, with 12.87 ± 0.06 MBq recovered at column outlet for a 12.2 MBq injected activity. The addition of radio-impurities in known quantities validated the accuracy of the method (differences between measured RCP and theoretical RCP ranging from 101.57% to 105.52%). CV% of RCP and tr values over 12 measures of a single batch were respectively <0.11% and <0.12%, which confirmed the repeatability of the method. Forced degradation conditions in the presence of

acid, base, oxidative stress or heating led to the formation in situ of impurities with a tr largely different from the analyte, confirming the specificity of the method. LOQ and LOD were 0.68 and 0.21 MBq/mL, respectively, and the radiodetector response was linear from 2 to 300 MBq/mL (R^2 = 0.9977). Robustness was found to be limited as the mean tr values varied by -4.8% when the column was heated to 50 °C instead of 25 °C.

Conclusion and Relevance A radio-HPLC method for the quality control of ^{177}Lu-PSMA-617 was validated and can be used for in-house preparations for preclinical purposes of this radioactive drug.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest.

3PC-041 PUBLIC PRODUCTION OF THERAPEUTIC BACTERIOPHAGES

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Background and Importance To stern antibiotic resistance -the death toll of which is predicted to reach 10 million deaths per year by 2050- new strategies are explored such as phage therapy. It takes advantage of the ability of bacteriophages or phages – viruses of bacteria – to infect, replicate and lyse their host.

Aim and Objectives PHAG-ONE project (20-PAMR-0009) allowed the creation of an Etablissement Français des Phages Thérapeutiques (EFPT) working with French hospitals to treat patients who reached therapeutic dead ends. This work details the future approach for hospital production of phage suspensions.

Material and Methods Selection of production host: An *in-silico* approach, based on a bioinformatics pipeline, was developed to select the bacterial strains the most free of virulence factors and resistances.

Selection of high therapeutic potential phages: Phages were sampled from their natural environment, identified by genetic sequencing; their activity range was tested on a bacterial panel representative of the clinical and genetic diversity of the pathogen. Phages with broad activity spectrum and complementary activities were selected for further pharmaceutical development.

Results

Production After amplification on the selected hosts, phages were purified by tangential flow filtration and ultrafiltration. The output was qualified as an active pharmaceutical ingredient (API) authorised by the French regulatory health agency (ANSM). This API can enter hospital preparations.

Formulation and quality control The excipients for the hospital preparations were selected to (i) enhance the phage suspension stability and (ii) be suitable for clinical use. The quality controls target (i) the phage identity and activity; (ii) the risks associated with the administration route; (iii) the risks associated with the production process. The hospital preparation's stability is explored following both ICH and predictive approaches.

Conclusion and Relevance The authorisations to produce phage API and hospital preparations of phage suspensions will be asked according respectively to the fabrication (part 2 and appendix 2) and preparation good practices and to the future general chapter 'Phage therapy active substances and medicinal products for human and veterinary use (5.31)'. Inspired by the French blood establishment, EFPT's purpose will be to offer phage suspensions against multi resistant bacteria or to treat patients with infectious recurrences and other bacterial therapeutic dead ends in a personalised approach.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest.

3PC-042 STERILE AND NON-STERILE COMPOUNDING: RISK ANALYSIS AND IMPROVEMENT MEASURES

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Background and Importance Drug compounding errors can result in patient harm. Hence, the importance of reviewing formulations to ensure their quality and safety.

Aim and Objectives To analyse the risk derived from our current process of sterile and non-sterile compounding, through error records registered for 1 year, and to list and prioritise measures to solve them.

Material and Methods A descriptive study, including errors related to sterile and non-sterile compounding (non-parenteral nutrition, non-chemotherapy) registered from October 2022 to September 2023, was conducted. Errors were classified according to their causes. Error's severity was determined subjectively by the pharmaceutical team.

A brainstorming session was organised, with technicians and the pharmacist leading safety, to discuss the critical points of the entire process. An Ishikawa diagram was created to visually capture the critical points. Improvement measures to reduce risk of errors were listed and prioritised by feasibility and effectiveness.

Our current process consists of: – Organisation: Outlook schedule, email requests, electronic and paper prescriptions – Non-sterile compounding: managed through Magisfor® software – Sterile compounding: managed through processing forms.

Results Sixty-four errors were detected: seven (10.9%) due to organisational causes, six (9.4%) derived from software/processing forms, eight (12.5%) compounding process, five (7.8%) quality control, five (7.8%) packaging, 23 (35.9%) labelling, seven (10.9%) storage, and three (4.7%) due to validation causes.

Twenty-five (39%) errors were considered severe. Errors were mainly detected by pharmacists during the validation process (n=54, 84%), others by technicians/nurses.

In total, 25 main critical points were detected through the Ishikawa diagram.

Improvement measures that could be implemented are: