time, as was the presence of possible dimers at 6.0 ± 0.1 min (small chromatographic peak). Chromatographic analysis of the same samples stored at room temperature and protected from light in a refrigerator at 4°C indicated the absence of a peak at 6.1 ± 0.1, the shift of the main peak to 8.1 ± 0.1, and the detection of a new chromatographic peak at 9.5 ± 0.1.

Conclusions The results of this study indicated the absence of aggregate formation in bevacizumab 5 mg/ml during the period of monitoring (15 days) under the two storage conditions tested. Nevertheless, they clearly indicate some kind of break down.

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No conflict of interest.

TCH-026 LONG-TERM STUDY OF THE FORMATION OF AGGREGATES IN UNDILUTED CETUXIMAB 5 mg/ml

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Background Cetuximab (Erbitux) is a chimeric monoclonal IgG1 antibody, an epidermal growth factor receptor (EGFR) inhibitor, given by intravenous infusion for the treatment of metastatic colorectal cancer and head and neck cancer. Cetuximab is produced in a mammalian cell line (Sp2/0) by recombinant DNA technology.

Purpose To evaluate the stability of this therapeutic monoclonal antibody, i.e. cetuximab 5 mg/ml in solution for infusion, in terms of the formation of aggregates once the vial was open. The study was carried out for up to 15 days since the manufacturer only indicates chemical and physical in-use stability for up to 48 hours at 25ºC, if the solution was prepared in validated aseptic conditions.

Materials and Methods The study of the formation of the aggregates was carried out by using a size exclusion high performance liquid chromatography method with a diode array detection method (SE-HPLC-DAD. Two different storage conditions, i.e. refrigerated at 4°C and frozen at –20°C, were considered up to 15 days. Samples were characterised by chromatographic analysis immediately after the vial was opened. These chromatographic data were compared with those obtained on subsequent days. A stress study was also conducted.

Results Analysis of freshly-prepared samples enabled us to characterise cetuximab chromatographically by SE-HPLC-DAD. In the corresponding chromatograms monomers were clearly detected (peak at 6.77 ± 0.05 minutes of retention time) while dimers or aggregates (peaks at retention times near to 6 minutes or smaller) were absent. Chromatographic analysis of the same samples stored at room temperature and protected from light in a refrigerator at 4°C and frozen at –20°C over a 15-day period indicate the absence of any kind of aggregates.

Conclusions The results of this study indicated the absence of the aggregate formation in cetuximab 5 mg/ml during the period of monitoring (15 days) under the two storage conditions tested.

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No conflict of interest.

TCH-027 MEDIA FILL TO VALIDATE THE ASEPTIC PREPARATION OF SODIUM BICARBONATE INTRAVENOUS INFUSION

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Background Sodium Bicarbonate is an alkaline agent and is indicated for treating acute or chronic metabolic acidosis. The substance is unstable and when heated in solution it gradually changes into sodium carbonate. That' s why we prepared Sodium Bicarbonate Intravenous Infusion aseptically, according to the Standard Operating Procedure.

Purpose To validate the performance of aseptic processes used to produce our sterile product and to meet Good Manufacture Practice Requirements, i.e. to comply with the 'low', twice per year we are performing media fill (process simulation studies).

Materials and Methods Media fills are simulating the whole process in order to evaluate the sterility confidence of the process. Process simulations includes formulation (compounding), filtration and filling. Important factors in the process are: personnel (number, shift changes, fatigue), sterility test for the sterilised components (bottles, stoppers), filled volume per container (sufficient to wet all surfaces of the containers), frequency, media fill sizes, acceptance criteria, environmental monitoring. We select the growth medium and prepared the bulk media as the same process as routine production including filtering process and number of units (the batches is smaller than 1000). Than all units were incubated at 20–25° C for 14 days.

Results After the incubation period of the media filled containers they were visually examined for microbial growth. The contamination rate is zero, so, the accepted contamination rate is less then 0, 1%. (Contamination rate = Upper confidence limit/Number of filled units × 100)

Conclusions With media fill we evaluate the aseptic assembly and operation of the sterile equipment, qualified the operators, and assess our technique, and demonstrate that the environmental controls are adequate to meet the basic requirements necessary to produce Sodium Bicarbonate Intravenous Infusion by aseptic procesing.

No conflict of interest.

TCH-028 NEW BULSULFAN PROCEDURE TO IMPROVE BOTH PREPARATION AND ADMINISTRATION

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Background When pharmacy staff is not available, nurses used to prepare diluted busulfan solution from commercial vials just before administration because of its low stability. Doing this without protection may cause occupational exposure to this cytotoxic drug.

Purpose To devise a new protocol and perform a preliminary evaluation.

Materials and Methods Literature and technical studies were performed to choose the best devices. Nurses and physicians performed a clinical evaluation using a 5-item satisfaction form.

Results Medical devices containing polycarbonate must be avoided because of the interaction with N,N-dimethylacetamide used as an excipient. The new protocol consists of an individual kit with the commercial solution packed in a syringe, an infusion bag with the

exact volume of diluent and a closed system transfer device (CSTD). Nurses just have to dilute the solution into the bag under a laminar air-flow hood using the CSTD. Although 2-part syringe methods were found in the literature, 3-part syringes with limited contact between the elastomeric tip and busulfan solution (reference 62.8426, Codan) were chosen because leaks were observed with the 2-part syringes during the technical study. PhaSeal devices: Injector to close the syringes and a Connector-Luer for infusion bags were selected as CSTDs. All these devices are polycarbonate free.

7 new kits were prepared for a period of 8 days without contact. The results of the evaluation show that nurses and physicians (n = 14) were overall dissatisfied by the previous protocol (neither good nor bad: 35.7%, bad: 21.4% and very bad: 35.7%) while the majority preferred the new one (very satisfied: 28.6%, satisfied: 42.9%, neither good nor bad 7.14%, no response: 21.4%). Overall nurses and physicians answered that new modalities limit the risk of dose errors (93%) and occupational exposure (86%).

Conclusions Implementing this procedure has improved handling practise with good satisfaction.

No conflict of interest.

TCH-029 OUTCOMES EVALUATION OF AN INTERNATIONAL WORKGROUP ON ROBOTICS: A MULTICENTRE STUDY

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Background The growing demand for patient and operator safety in anticancer drug compounding led to an increasing demand for automation. As 18 hospitals have now introduced APOTEC Achemo, it became necessary to set up a round table at which all users could share their knowledge and expertise. Therefore, in 2009 a workgroup on robotics (named APOTECA Community) was established. Every year its members meet to share their needs with the manufacturer and assemble new ideas. The annual system upgrade is a consequence of the meeting. 160 new requirements, merged into 4 upgrades, have been collected up to now. The requirements can be classified into the following main topics: a friendlier user interface; software integration with medical health records; higher productivity.

Purpose To assess the results in terms of productivity following the 2012 upgrade within the APOTECA Community

Materials and Methods Five oncology pharmacies were selected for this study: University Hospital of Ancona, European Institute of Oncology, Romagna Cancer Institute, S. Camillo Hospital of Rome, Cleveland Clinic. The abovementioned pharmacies were monitored before and after the upgrade, as far as the monthly productivity with APOTEC Achemo is concerned.

Results The 5 hospitals together prepared an average of 4150 preps/month before the 2012 upgrade, while 6000 preps/month was surpassed after the installation. Productivity showed an average increase of 46%, ranging from 11% to 67%. This variability is closely correlated with the best practise and has been analysed for each case.

Conclusions The creation of a round table where the APOTEC-Achemo users share experiences and discuss best practise is playing an essential role in the continuous improvement of this innovative technology. The progress recorded after the latest upgrade in terms of productivity (+46%) is only one example of this powerful tool.

No conflict of interest.

TCH-030 PET/CT IMAGING WITH [11C]CHOLINE AS A RADIOPHARMACEUTICAL FOR THE DETECTION OF RECURRENT PROSTATE CANCER: A RELIABLE PRODUCTION METHOD AND QUALITY CONTROL

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Background PET/CT Imaging with the radiopharmaceutical [11C]-choline has become a useful tool in the detection of prostate cancer, mainly used in the assessment of treated patients presenting rising PSA and negative response after conventional imaging procedures. Tracer uptake on tumoral tissues is correlated to an increased synthesis of membrane substrates: [11C]-choline is trapped by phosphorylation taking part on phosphatidylcholine turnover. The sensitivity of this diagnostic method (almost 100%) is greater than CT or PET-[18F]FDG implying the superiority of the PET-choline procedure. PET-choline was first investigated in the late 1990s although no specific monographs are included in main Pharmacopoeias. The use of this powerful tracer is now based on Clinical Trials but, on September 2012, the FDA approved the production and use of 'Choline C11 Injection' to help the detection of recurrent prostate cancer.

Purpose To define the key role the pharmacist plays in the preparation of [11C]-choline IMPD for Clinical Trials, presenting the tracer production in the details. Quality Control for characterising the final product and releasing it as 'solutio iniectabilis' are also described.

Materials and Methods

cyclotron (Eclipse, Siemens)
Automatized synthesiser (ModularLab, Eckert Ziegler)
GMP grade reagents and disposables
[11C]labelling based on 'wet' methylation chemistry

Results [11C]carbon dioxide (50 GBq) was produced by cyclotron and delivered to the synthesiser placed in our radiopharmacy. Carbon dioxide was first reduced to methyl iodide, then dimethyl-aminoethanol was [11C]-methylated. Finally the product was purified and filtered obtaining 15 GBq of sterilised [11C]-choline (16 min total time and 30% yield). Radiochemical purity was higher than 98% and other CQs were performed in accordance with EPh [18F] FDG monograph.

Conclusions Due to the short half-life decay (20 min) [11C]-choline production must be performed in PET facilities with on-site cyclotron and radiopharmacy. We presented a reliable and safe method for producing [11C]-choline for 3–4 patients' PET scans.

No conflict of interest.

TCH-031 PHARMACIST EXPERIENCE IN CONTINUING IMPROVEMENT OF THE AUTOMATIC SYSTEM

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Background An annual meeting between the manufacturer of APOTECAchemo and all the users is held to share experience and discuss suggestions for best practise. The feedback collected during the meeting forms the basis for the next system upgrade aimed at increasing performance. Some improvements that we suggested were included in the 2012 upgrade and improved our productivity: a new procedure for reconstitutions; an extemporaneous picking list; faster communication between the management software and the robot; a more efficient vision system for identifying labels.