PP-004

QUALITY CONTROL ASSESSMENT OF CYTOTOXIC BAGS BY UV-RAMAN SPECTROMETRY

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1 BACKGROUND

About 6000 cytotoxic bags per year are compounded in the pharmaceutical unit of the University Hospital Pharmacy. Each bag was controlled by UV-Raman spectrometry.This analytical technique presents many advantages for a better efficiency: identification and quantification results, a short time of analysis (only 2 minutes) and a sample acceptable volume (1mL).

2 PURPOSE

The aim of this study was to evaluate the quality control of cytotoxic bags compounded and analyzed during 11 months from November 2013 to October 2014 by UV-Raman spectrometry.

3 MATERIAL AND METHODS

All the drugs and solvents were identified and a five points calibration linear curve was realized. Analytical method for each cytotoxic molecule was validated for between-day, within –day reproducibility and accuracy (less than 5% RSD for acceptance) following ICH recommendations. A quality control of each drug was analyzed every week to check instrumentation and calibration. For 11 months, cytotoxic bags were routinely produced and then controlled by UV-Raman spectrometry. Criteria acceptance for cytotoxic bags production is +/- 10% deviation. Tolerance occurred when deviation was between 10 and 15 %. If +/- 15% deviation was found, status was rejected.

4 RESULTS

4838 cytotoxic bags were produced and analyzed for 11 months. 14 cytotoxic drugs were analyzed by UV-Raman: carboplatin, cisplatin, cyclophosphamide, dacarbazine, docetaxel, doxorubicin, etoposide, ganciclovir, gemcitabine, ifosfamide, oxaliplatin, paclitaxel, pemetrexed, vinorelbine. 92.1% of cytotoxic bags passed in the concentration range of ±10 %; 5.2% in the tolerance range (±15 %) and 2.0% rejected with difference of more ± 15 %. The most non-compliance preparation were: doxorubicin (18.8 %), cyclophosphophosphamide (14.3 %) and ifosfamide (11.1 %). Only 0.6 % of analysis resulted in a misidentification of the molecule.

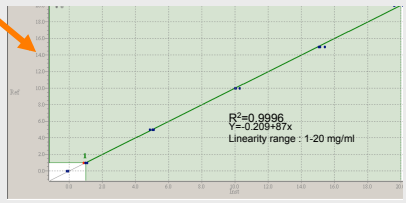
5 CONCLUSIONS

This study shows that the quality of cytotoxic bags compounding is satisfactory and that the UV-Raman is an adequate technique to analyze drugs. However these results also highlight defects of preparation of some cytotoxic bags which lead for example to enhance reconstitution time of cyclophosphamide powder and to improve some preparations protocols.
This approach goes into a continuous process of quality improvement of drug preparations in hospital pharmacy.

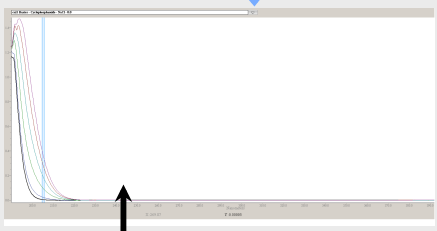
QC PREP® UV-RAMAN spectrometer

Method validation

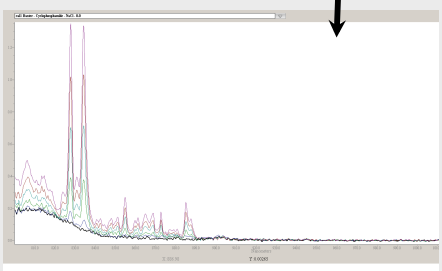
Calibration curve of cyclophosphamide



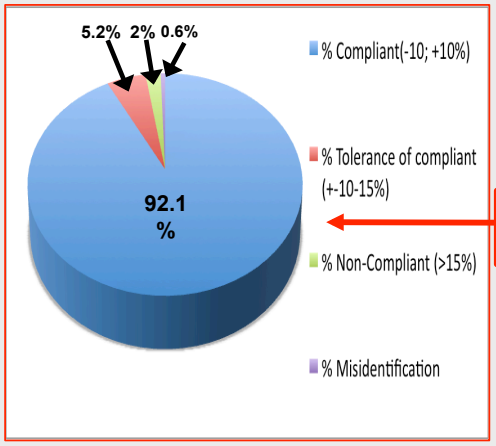
Sample analysis



UV spectrum and Raman spectrum of Cyclophosphamide



% of Compliant cytotoxic bags from 4838 analysis by UV-RAMAN spectrometry



Results of deviation of cytotoxic agent

Molecule	Number of bags	Compliant (-10; +10%)	Tolerance of compliance (+-10-15%)	Non-compliant (>+-15%)	Misidentification
Carboplatine (%)	654	642 (98)	5 (1)	7 (1)	0
Cisplatine (%)	313	299 (96)	11 (3)	3 (1)	0
Cyclophosphamide (%)	147	106 (72)	20 (14)	21 (14)	0
Dacarbazine (%)	18	18 (100)	0	0	0
Doxetaxel (%)	156	156 (100)	0	0	0
Doxorubicine (%)	16	11 (69)	2 (13)	3 (19)	0
Etoposide (%)	809	774 (96)	22 (3)	11 (1)	2 (0.2)
Ganciclovir (%)	304	261 (86)	27 (9)	8 (2)	8 (2)
Gemcitabine (%)	380	318 (84)	42 (11)	13 (3)	7 (2)
Ifosfamide (%)	18	13 (72)	2 (11)	2 (11)	1 (6)
Oxaliplatine (%)	13	11 (85)	2 (15)	0	0
Paclitaxel (%)	1223	1109 (91)	94 (8)	18 (2)	2 (0.2)
Pemetrexed (%)	347	316 (91)	18 (5)	10 (3)	3 (1)
Vinorelbine (%)	440	424 (96)	8 (2)	2 (0.5)	6 (1.4)
Total	4838	4458	253	98	29
%	100	92.1	5.2	2.0	0.6