TCH-044 STERILITY TESTING USING A RAPID MICROBIOLOGICAL METHOD FOR BATCH PRODUCTION OF CYTOTOXIC DRUGS IN A HOSPITAL PHARMACY

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Background To improve the quality of sterile cytotoxic drug preparation in hospital pharmacy, we implemented batch production of standardised doses of 11 cytotoxics and 1 monoclonal antibody using the Repeater pump (Baxa, Baxter). In accordance with French good manufacturing practise for hospital pharmacies [1], physicochemical and sterility tests have to be implemented for batch release.

Purpose To investigate the possible use of a rapid microbiological method (BD Bactec) for sterility testing of batches of cytotoxic drugs.

Materials and Methods Taking into account the possible inhibition of microorganism growth with cytotoxics [2–4], we investigated the detection of microbial growth of cytotoxic bags with the Bactec system (CO_2 detection by fluorescence) when inoculated with <100 Colony-Forming Units (CFUs) of 4 microorganisms recommended in the European Pharmacopeia [5] (Staphylococcus aureus (SA), Pseudomonas aeruginosa (PA), Bacillus subtilis (BS) and Candida albicans (CA)) and 3 microorganisms usually found in clean rooms (Staphylococcus epidermidis (SE), Escherichia coli (EC) and Enterococcus faecalis (EF)).

Results All species were detected in only cyclophosphamide and trastuzumab, while conversely 5 fluorouracil (5FU) inhibited the growth of all microbial species. For 5FU, the use of an alternative device (Bact/Alert, Biomerieux) with CO_2 detection by colorimetric method or the 1/10 dilution of the 5FU solution, allowed growth to recover for Staphylococcus species, Candida albicans and Escherichia coli. For most of the remaining drugs, Pseudomonas aeruginosa and Bacillus subtilis seemed to be routinely inhibited.

Conclusions Further dilutions of cytotoxic bags or use of Bact/Alert are planned to improve the results. Moreover, the combination of sterility tests with the Bacterial Endotoxin Test [6–7] would help improve the results for Gram-negative bacteria.

Abstract TCH-044 Table 1

Drug	Device	Concentration (mg/ml)	SA	PA	BS	CA	SE	EC	EF
	Bactec	22	–	–	–	–	–	–	–
5 Fluorouracil	Bactec	2.2	–	–	–	+	–	+	–
	Bact/Alert	22	+	–	–	+	+	–	–
	Bactec	10	–	+	–	+	–	–	–
Gemcitabine	Bactec	1	–	+	–	+	–	+	–
	Bact/Alert	10	–	+	–	+	–	+	–
Carboplatin	Bactec	2	+	+	+	+	+	–	+
Cisplatin	Bactec	0.2	+	–	–	+	+	–	+
Oxaliplatin	Bactec	0.5	+	–	+	+	+	+	+
Epirubicin	Bactec	2	–	–	–	+	–	+	+
Cyclophosphamide	Bactec	4	+	+	+	+	+	+	+
Docetaxel	Bactec	0.68	+	–	–	+	+	ND	+
Paclitaxel	Bactec	0.6	+	–	–	+	+	+	+
Etoposide phosphate	Bactec	1	+	–	+	+	+	+	+
Irinotecan	Bactec	1.15	+	–	+	+	+	+	+
Trastuzumab	Bactec	2.25	+	+	+	+	+	+	+

ND: Not Determined

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No conflict of interest.

TCH-045 SUITABILITY OF A SENSOR-DRIVEN, SINGLE-USE MICRO DOSING VALVE FOR VOLUMETRIC DISPENSING IN A MODULARLY ASSEMBLED MULTI-CHANNEL COMPOUNDER

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Background Major drawbacks of commercially available compounders are expensive prices, large-scale architecture (24 channels), restricted country support, and gravimetric dosing requiring periodically defined densities and flow factors. However, total parenteral nutrition (TPN) is prescribed in weights or moles of ingredients per volume.

Purpose To evaluate the suitability of a dosing unit formerly developed for inkjet printing and biotechnology for pharmaceutical compounding applications

To perform a feasibility study of a low-cost multi-channel compounder

Materials and Methods Applicability and practicability of the device was assessed by a focus group of researchers and practitioners. Criteria were mainly dosing accuracy, material characteristics, flexibility in module assembling, and predictable cost.

Results Features of a novel modularly-assembled multi-channel dosing unit, formerly designed for inkjet and media dosing in printers and bioreactors, were appraised for suitability for compounding applications. The core of the dosing unit consists of multiple autoclavable, chemically resistant, highly precise volumetric dispensing valves. 3 integrated flow rate sensors are used to measure 2 differential pressures, which permits temperature and viscosity-independent dosing (patent P7711CH01). The pressure above the valve amounts to 500 ± 5 mbar. An electronic valve driver controls the valves to microseconds. Media are transferred as single drops of 0.5 µl by a feeder into a mixing chamber. Exact dosing is guaranteed over a wide range, from µl to dl. The valve was successfully tested in field tests with micro bioreactors (patent CH702769A2). A prototype device for preparing all-in-one TPN bags is presently under construction, together with an electronic interface to patient and administration databases. Further options under development are nanodosing, integration of valves and sensors, as well as miniaturisation to obtain an affordable single-use device.

Conclusions The sensor-driven valve is suitable for use in a compounder for individual liquid preparations. The next step of assembling a prototype compounder is ongoing and aims to increase