

# Cytotoxic surface contamination in a robotic system compared with manual preparation

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## Background

The preparation of cytotoxic drugs involves the occupational risk of contamination by aerosolized drug product or contact contamination.

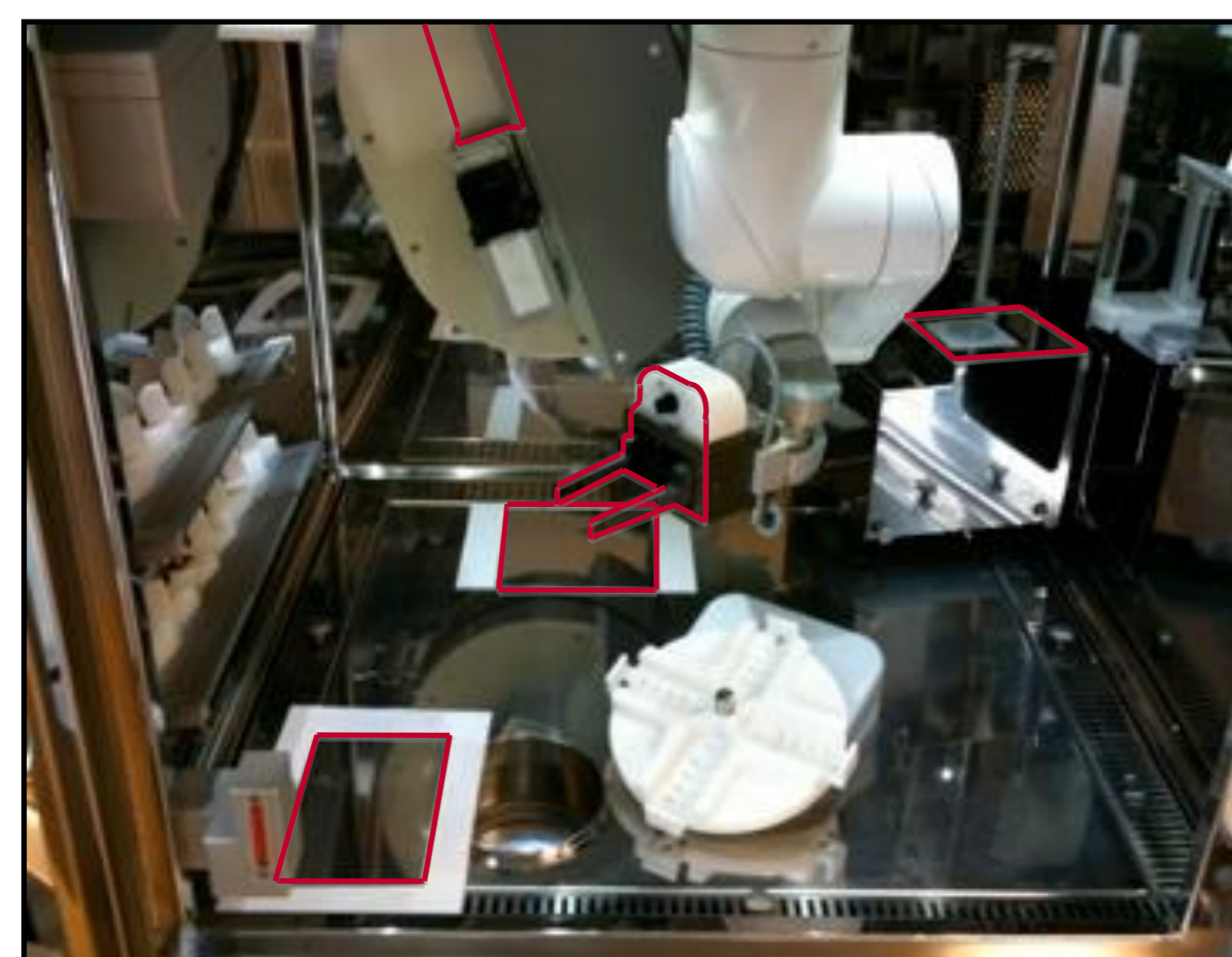
To work with a robot system could be an good option to reduce the operator exposure in assuming that automation leads to less contamination than the manual preparation in a workbench.



## Purpose

To compare the surface contamination with cytotoxic drug substances during automated preparation and during manual preparation.

## Materials and Methods

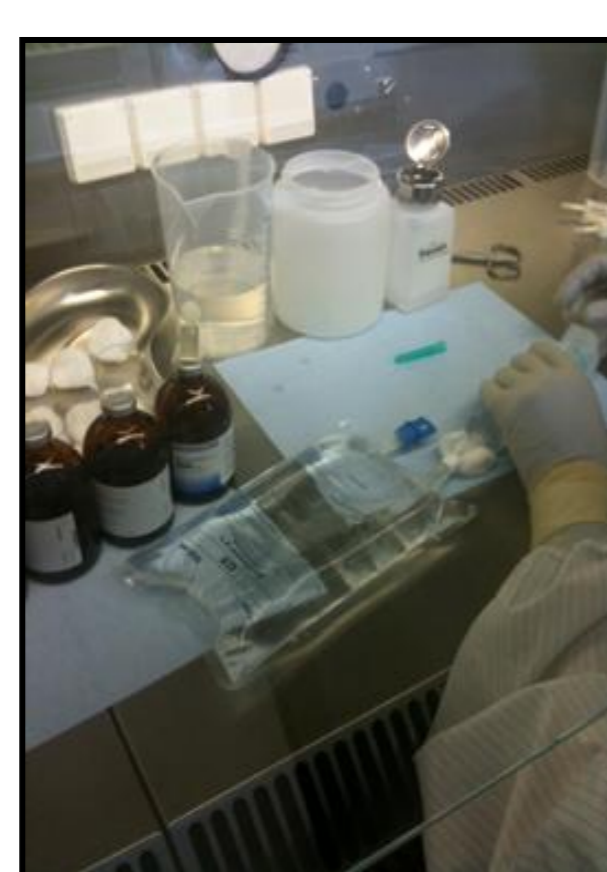


The contamination level of 5 predetermined areas inside the CytoCare™ cabinet was investigated with swab tests.

All surfaces were swabbed after the cleaning procedure and after finishing the preparation process.

In the first series, 15 bags of 5-FU and 15 bags of platinum containing cytotoxic drugs were prepared during two consecutive days:

- 15 x 5-FU 1200 mg ad 500 ml (day 1)
- 5 x cisplatin 40 mg ad 500 ml (day 2)
- 5 x carboplatin 450 mg ad 500 ml (day 2)
- 5 x oxaliplatin 120 mg ad 500 ml (day 2)



A second series was prepared and in addition the outer surface of each bag was swabbed.

In parallel, 15 bags of 5-FU and 15 bags of platinum containing cytotoxic drugs were prepared manually during two consecutive days and the surface contamination was studied.

4 specific areas of the laminar air flow, the gloves of the technician and all bags prepared were swabbed by the same method.

5-FU samples were analysed by gas chromatography / mass spectrometry and platinum samples were analysed by voltammetry after UV-digestion according to a known method. [Schierl R, et al.]



## Results

Interpretation of the results with Threshold Guidance Values

Results	Platinum (pg/cm <sup>2</sup> )	5-FU (pg/cm <sup>2</sup> )
Better than 50 % of all the samples	< 3,0	< 3,0
Between 50 and 75 %	≤ 4,0	≤ 30,0
Worse than 75 % of all the samples	> 4,0	> 30,0

Limits of detections:  
Platinum: nn = below 0,02 ng/sample

5-FU: nn = below 0,2 ng/sample

## Results

### Contamination in the Laminar Air Flow workbench:

Place of sampling	5-FU (pg/cm <sup>2</sup> )	Platinum (pg/cm <sup>2</sup> )
LAF right ((20*20)cm <sup>2</sup> )	1,3	1,3
Preparation-mats compounding ((20*20)cm <sup>2</sup> )	1,3	0,1
Preparation-mats vials ((13*20,5)cm <sup>2</sup> )	1,1	0,1
LAF left ((20*20)cm <sup>2</sup> )	1,1	0,6
Gloves (ca. 4*(10*10)cm <sup>2</sup> )	1,0	0,1
Blank value	-	-
LAF right ((20*20)cm <sup>2</sup> )	1,4	1,4
Preparation-mats compounding ((20*20)cm <sup>2</sup> )	1 725 000,0	0,2
Preparation-mats vials ((13*20,5)cm <sup>2</sup> )	67,4	16,7
LAF left ((20*20)cm <sup>2</sup> )	1,1	0,3
Gloves (ca. 4*(10*10)cm <sup>2</sup> )	726,5	34,5
Blank value	-	-

Place of sampling	5-FU (pg/cm <sup>2</sup> )	Place of sampling	Platinum (pg/cm <sup>2</sup> )
Bag 01 5-FU 2*(10*20)cm <sup>2</sup>	1,3	Bag 01 Cisplatin 2*(10*20)cm <sup>2</sup>	0,9
Bag 02 5-FU 2*(10*20)cm <sup>2</sup>	10	Bag 02 Cisplatin 2*(10*20)cm <sup>2</sup>	0,8
Bag 03 5-FU 2*(10*20)cm <sup>2</sup>	13	Bag 03 Cisplatin 2*(10*20)cm <sup>2</sup>	8,2
Bag 04 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 04 Cisplatin 2*(10*20)cm <sup>2</sup>	1,5
Bag 05 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 05 Cisplatin 2*(10*20)cm <sup>2</sup>	1,3
Bag 06 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 06 Carboplatin 2*(10*20)cm <sup>2</sup>	0,5
Bag 07 5-FU 2*(10*20)cm <sup>2</sup>	1,3	Bag 07 Carboplatin 2*(10*20)cm <sup>2</sup>	1,1
Bag 08 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 08 Carboplatin 2*(10*20)cm <sup>2</sup>	0,8
Bag 09 5-FU 2*(10*20)cm <sup>2</sup>	1,3	Bag 09 Carboplatin 2*(10*20)cm <sup>2</sup>	1,3
Bag 10 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 10 Carboplatin 2*(10*20)cm <sup>2</sup>	47,8
Bag 11 5-FU 2*(10*20)cm <sup>2</sup>	19,5	Bag 11 Oxaliplatin 2*(10*20)cm <sup>2</sup>	0,8
Bag 12 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 12 Oxaliplatin 2*(10*20)cm <sup>2</sup>	0,9
Bag 13 5-FU 2*(10*20)cm <sup>2</sup>	10,8	Bag 13 Oxaliplatin 2*(10*20)cm <sup>2</sup>	1
Bag 14 5-FU 2*(10*20)cm <sup>2</sup>	13,8	Bag 14 Oxaliplatin 2*(10*20)cm <sup>2</sup>	2,3
Bag 15 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 15 Oxaliplatin 2*(10*20)cm <sup>2</sup>	1
Blank value	-	Blank value	-

### Contamination in the CytoCare™ cabinet:

Place of sampling	5-FU (pg/cm <sup>2</sup> )	Platinum (pg/cm <sup>2</sup> )
Balance ((15*17,5)cm <sup>2</sup> )	10,9 [2,2 - 19,6]	0,9 [0,4 - 1,4]
Floor under the shelves ((13,5*20)cm <sup>2</sup> )	10,9 [2,2 - 19,6]	5,2 [4,9 - 5,4]
Syringes' holder (ca. 400cm <sup>2</sup> )	9,9 [7,8 - 12,0]	5,7 [0,9 - 10,4]
Floor under the syringes' holder ((20*20)cm <sup>2</sup> )	17,6 [2,3 - 33,0]	14,6 [8,7 - 20,6]
Robotic arm (ca. 180cm <sup>2</sup> )	1 196,7 [601,7 - 1 791,7]	4,7 [3,0 - 6,4]
Blank value	-	-
Balance ((15*17,5)cm <sup>2</sup> )	87,7 [3,0 - 172,2]	4,8 [3,7 - 5,9]
Floor under the shelves ((13,5*20)cm <sup>2</sup> )	74,3 [3,0 - 146,6]	11 [7,2 - 14,8]
Syringes' holder (ca. 400cm <sup>2</sup> )	1,1	29,8 [1,6 - 58,0]
Floor under the syringes' holder ((20*20)cm <sup>2</sup> )	625 001,1 [2,3 - 1 250 000,0]	24,5 [13,6 - 35,6]
Robotic arm (ca. 180cm <sup>2</sup> )	1 176,6 [428,9 - 3 124,2]	61,8 [8,1 - 114,4]
Blank value	-	-

Place of sampling	5-FU (pg/cm <sup>2</sup> )	Place of sampling	Platinum (pg/cm <sup>2</sup> )
Bag 01 5-FU 2*(10*20)cm <sup>2</sup>	8,8	Bag 01 Cisplatin 2*(10*20)cm <sup>2</sup>	1,3
Bag 02 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 02 Cisplatin 2*(10*20)cm <sup>2</sup>	0,9
Bag 03 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 03 Cisplatin 2*(10*20)cm <sup>2</sup>	3,2
Bag 04 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 04 Cisplatin 2*(10*20)cm <sup>2</sup>	0,2
Bag 05 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 05 Cisplatin 2*(10*20)cm <sup>2</sup>	0,3
Bag 06 5-FU 2*(10*20)cm <sup>2</sup>	560,5	Bag 06 Carboplatin 2*(10*20)cm <sup>2</sup>	0,3
Bag 07 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 07 Carboplatin 2*(10*20)cm <sup>2</sup>	0,2
Bag 08 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 08 Carboplatin 2*(10*20)cm <sup>2</sup>	0,2
Bag 09 5-FU 2*(10*20)cm <sup>2</sup>	242,5	Bag 09 Carboplatin 2*(10*20)cm <sup>2</sup>	0,1
Bag 10 5-FU 2*(10*20)cm <sup>2</sup>	11,5	Bag 10 Carboplatin 2*(10*20)cm <sup>2</sup>	0,4
Bag 11 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 11 Oxaliplatin 2*(10*20)cm <sup>2</sup>	0,1
Bag 12 5-FU 2*(10*20)cm <sup>2</sup>	150,8	Bag 12 Oxaliplatin 2*(10*20)cm <sup>2</sup>	0,1
Bag 13 5-FU 2*(10*20)cm <sup>2</sup>	1,1	Bag 13 Oxaliplatin 2*(10*20)cm <sup>2</sup>	0,3
Bag 14 5-FU 2*(10*20)cm <sup>2</sup>	24,8	Bag 14 Oxaliplatin 2*(10*20)cm <sup>2</sup>	0,5
Bag 15 5-FU 2*(10*20)cm <sup>2</sup>	95,5	Bag 15 Oxaliplatin 2*(10*20)cm <sup>2</sup>	24,5
Blank value	-	Blank value	-

Contamination with cytotoxics was observed in the working area of the CytoCare™ and on the outer surface of several products automatically compounded.

The contamination levels were similar or higher by preparation in the robot than in the manual preparation process.

## Conclusions

The cleaning procedure of the CytoCare™ turned out to be insufficient and must be improved.

Further investigations are necessary to identify the origin(s) of the contamination and to reduce them.

## Reference

Schierl R, et al., Guidance Values for Surface Monitoring of Antineoplastic Drugs in German Pharmacies, Ann. Occup. Hyg., Vol. 53, No. 7, pp. 703–711, 2009.