Chemical Contamination by Cytostatic Drugs in Pharmacies – Data from Germany

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Motivation

Safe (low risk) handling of cytostatic drugs

Helping personnel
- to find weak points and
- to improve procedures
Several guidelines and brochures available ....

Biological monitoring not recommended, but environmental contaminations should be monitored.
Wipe sampling procedure - LMU
(validated since 2000)

- Delivery of ``wipe sampling kit``
- Wiping by pharmacy personnel following our manual
- Over night shipping of samples
- Analysis in our laboratory
- Report with recommendations
## Figures of merits

<table>
<thead>
<tr>
<th>substance</th>
<th>solvent for wiping</th>
<th>method of determination</th>
<th>detection limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platinum</td>
<td>HCl (0.5 %)</td>
<td>voltammetry</td>
<td>0.02 0.05</td>
</tr>
<tr>
<td>5-Fluorouracil</td>
<td>methanol</td>
<td>GC/MS</td>
<td>0.1 0.3</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>ethyl acetate</td>
<td>GC/MS</td>
<td>1 3</td>
</tr>
<tr>
<td>Ifosfamide</td>
<td>ethyl acetate</td>
<td>GC/MS</td>
<td>1 3</td>
</tr>
</tbody>
</table>
Wipe samples from 103 pharmacies (62 % hospitals)

<table>
<thead>
<tr>
<th>Location</th>
<th>FU n</th>
<th>PT n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Floor BSC</td>
<td>207</td>
<td>188</td>
</tr>
<tr>
<td>Floor</td>
<td>61</td>
<td>42</td>
</tr>
<tr>
<td>Storage</td>
<td>114</td>
<td>128</td>
</tr>
<tr>
<td>Pre-Prep</td>
<td>246</td>
<td>190</td>
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<tr>
<td>BSC</td>
<td>107</td>
<td>86</td>
</tr>
<tr>
<td>Post-Prep</td>
<td>230</td>
<td>170</td>
</tr>
<tr>
<td>Waste</td>
<td>51</td>
<td>53</td>
</tr>
<tr>
<td>Desk inside</td>
<td>44</td>
<td>48</td>
</tr>
<tr>
<td>Desk outside</td>
<td>87</td>
<td>48</td>
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<tr>
<td><strong>Σ</strong> 1147</td>
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<td></td>
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<tr>
<td><strong>Σ</strong> 953</td>
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</table>
Results of wipe samples - Contamination by fluorouracil (FU)

1147 samples
74 % > DL
Results of wipe samples - Contamination by fluorouracil (FU)

MEWIP: LOD

Results of wipe samples - Contamination by fluorouracil (FU)

MEWIP: LOD
Example (1) floor contamination

4 broken vials Holoxan 2 g (liquid)
Correct use of spill kit

14 days later: wipe samples
Place of accident: 260 000 pg/cm² Ifosfamid
5 m away: 37 500 pg/cm² Ifosfamid

Cleaning with methanol
Place of accident: 92 000 pg/cm² Ifosfamid
5 m away: 3 000 pg/cm² Ifosfamid

4 months normal daily cleaning
Place of accident: 450 pg/cm² Ifosfamid
5 m away: 50 pg/cm² Ifosfamid
Contamination of Vials
Pt contamination

ng/vial

Lot

n = 7 13 23 5 2 8 23
Results of wipe samples - Contamination by platinum (PT)

<table>
<thead>
<tr>
<th>pg/cm²</th>
<th>4.0</th>
<th>3.5</th>
<th>3.0</th>
<th>2.5</th>
<th>2.0</th>
<th>1.5</th>
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<tbody>
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Floor BSC, Floor, Storage, Pre-Prep, BSC, Post-Prep, Waste, Desk inside, Desk outside
We would like to propose a TGV Threshold Guidance Value
Threshold guidance values for Fluourouracil

pg/cm²

Floor BSC | Floor | Storage | Pre-Prep | BSC | Post-Prep | Waste | Desk inside | Desk outside

48 | 09 | 46 | 46 | 35 | 33 | 11 | 13 | 16

75.Perc.

50.Perc.
Threshold guidance values for Platinum

pg/cm²

31  3  33  30  31  23  18  3  2

Floor BSC  Floor  Storage  Pre-Prep  BSC  Post-Prep  Waste  Desk inside  Desk outside

75.Perc.

50.Perc.
Are those TGVs practical ???
Monitoring example (1) for FU

<table>
<thead>
<tr>
<th>Sampling</th>
<th>pre prep</th>
<th>storage</th>
<th>floor</th>
<th>post prep</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>950</td>
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</table>
Monitoring example (1) for FU

- Sampling:
  - 1
  - 2
  - 3
  - 4
  - 5
  - 6
  - 7

- FU pg/cm²:
  - pre prep
  - storage
  - floor
  - post prep

- FU values:
  - Sampling 1: pre prep (100)
  - Sampling 2: storage (1)
  - Sampling 3: floor (60)
  - Sampling 4: post prep (10)
  - Sampling 5
  - Sampling 6
  - Sampling 7

- Graph shows the distribution of FU pg/cm² across different sampling points and categories.
Monitoring example (2) for PT

![Bar chart showing Pt pg/cm² for sampling points 1 to 5. The chart includes data for pactosafe, floor, desk, and office. The values range from 0 to 1.0.]

- Sampling 1: pactosafe 0.6, floor 0.4, desk 0.3, office 0.1
- Sampling 2: pactosafe 0.9, floor 0.7, desk 0.4, office 0.2
- Sampling 3: pactosafe 0.5, floor 0.3, desk 0.4, office 0.1
- Sampling 4: pactosafe 0.8, floor 0.6, desk 0.5, office 0.2
- Sampling 5: pactosafe 0.7, floor 0.5, desk 0.4, office 0.1

The highest value is at Sampling 2 with pactosafe at 0.9.
Take home message

Wipe samples are fine tool for

- documentation of working practices
- detection of contaminations
- showing improvements

Our results show

- the need of good detection limits (maybe more important than many different drugs)
- that TGVs are possible and helpful
- a positive response by local staff
Many thanks to my co-workers

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