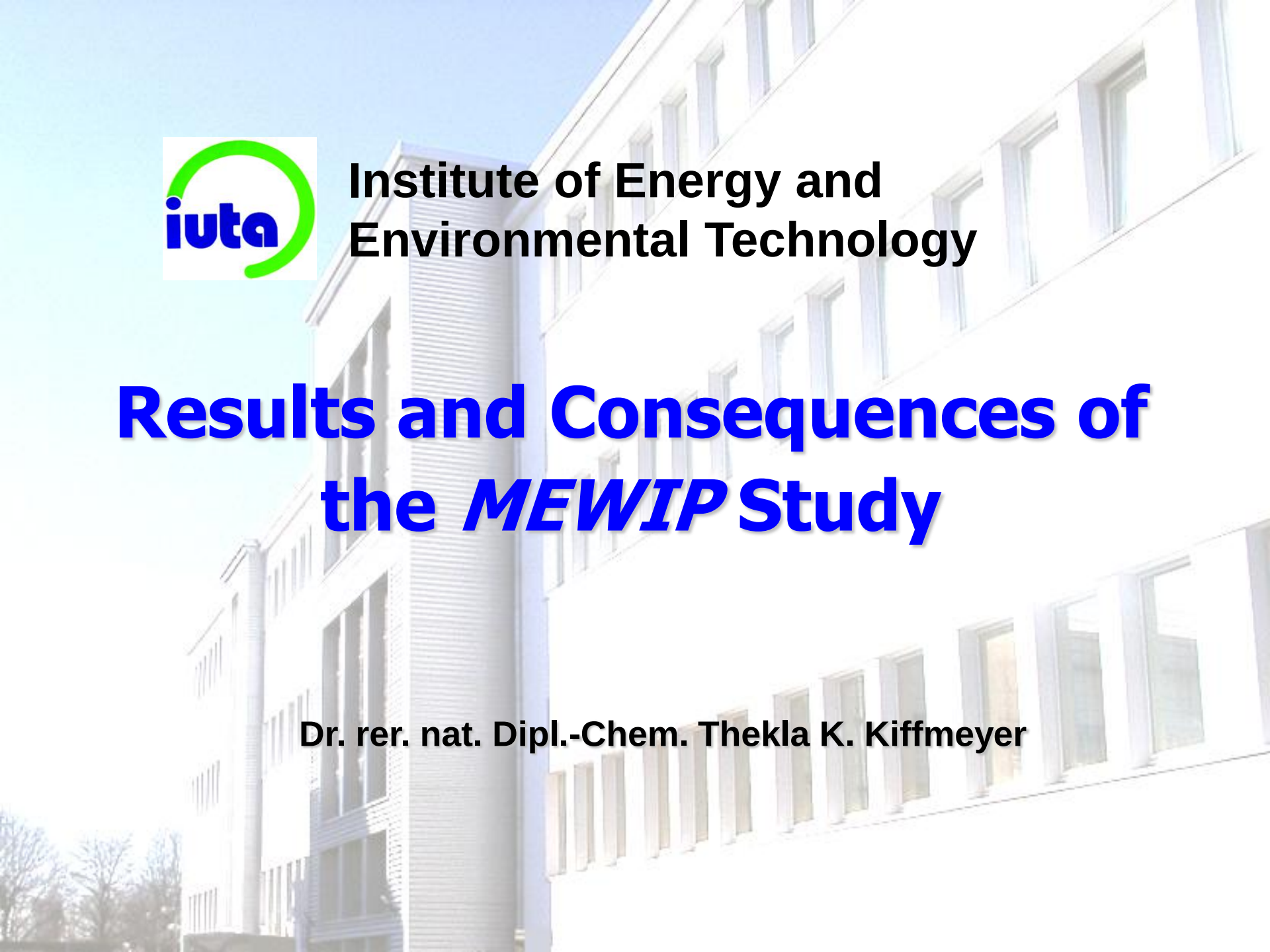


Institute of Energy and Environmental Technology

Results and Consequences of the *MEWIP* Study

Dr. rer. nat. Dipl.-Chem. Thekla K. Kiffmeyer

Outline

1. Introduction
2. Monitoring procedures
3. The MEWIP-Study:
   - Background
   - Aims
   - Methods
   - Results
   - Consequences
4. Cleaning procedures:
   - Surfaces
   - Textiles
   - Vials
   - Spill management

IUTA: Facts and Figures

History

1989	Foundation as Institute of Environmental Technology and Environmental Analysis e.V.
1991	Institute in cooperation with the University Duisburg-Essen
1998	Renamed as Institute of Energy and Environmental Technology

Institute of Energy and Environmental Technology
Bliersheimer Str. 60
47229 Duisburg
Germany

Internet: www.iuta.de

Facts & Figures (2007):

Employees	150
Office/Laboratory space	2.400 m²
Technicums area	4.000 m²
Turnover	6,5 Mio €

Activities of IUTA related to hazardous drugs

- Development and application of monitoring procedures
- Improvement of technical protective equipment, esp. BSCs
- Testing and improvement of cleaning methods
- Development of sensitive, validated analytical methods
- Investigation of occurrence and fate in the environment
- Treatment of hospital and municipal waste water
- Development of self decontaminating surfaces
- Investigation of evaporation and air contamination
- Development of rapid tests for surface contamination
- Scientific colloquia and training seminars

Monitoring tools in occupational safety

Ambient Monitoring

Determination of the original substance or relevant metabolites at the workplace

Wipe sampling from hard surfaces: work tops, BSCs, isolators, shelves, transport boxes, waste containers, fridges, vials, applications, handles, switches, telephone, keyboards, …

Elution of textiles: working and cleaning clothes, bed linen, …

Air measurements: particles and gas phase

Wipe sampling from skin and hair

Biological Monitoring

Biomonitoring

Determination of the original sub-stance or relevant metabolites in urine, blood, serum, sweat, …

Cytogenetic monitoring

Early genotoxic effects: chromoso-mal aberrations, Sister chromatid exchange, micronuclei, …

Epidemiological studies

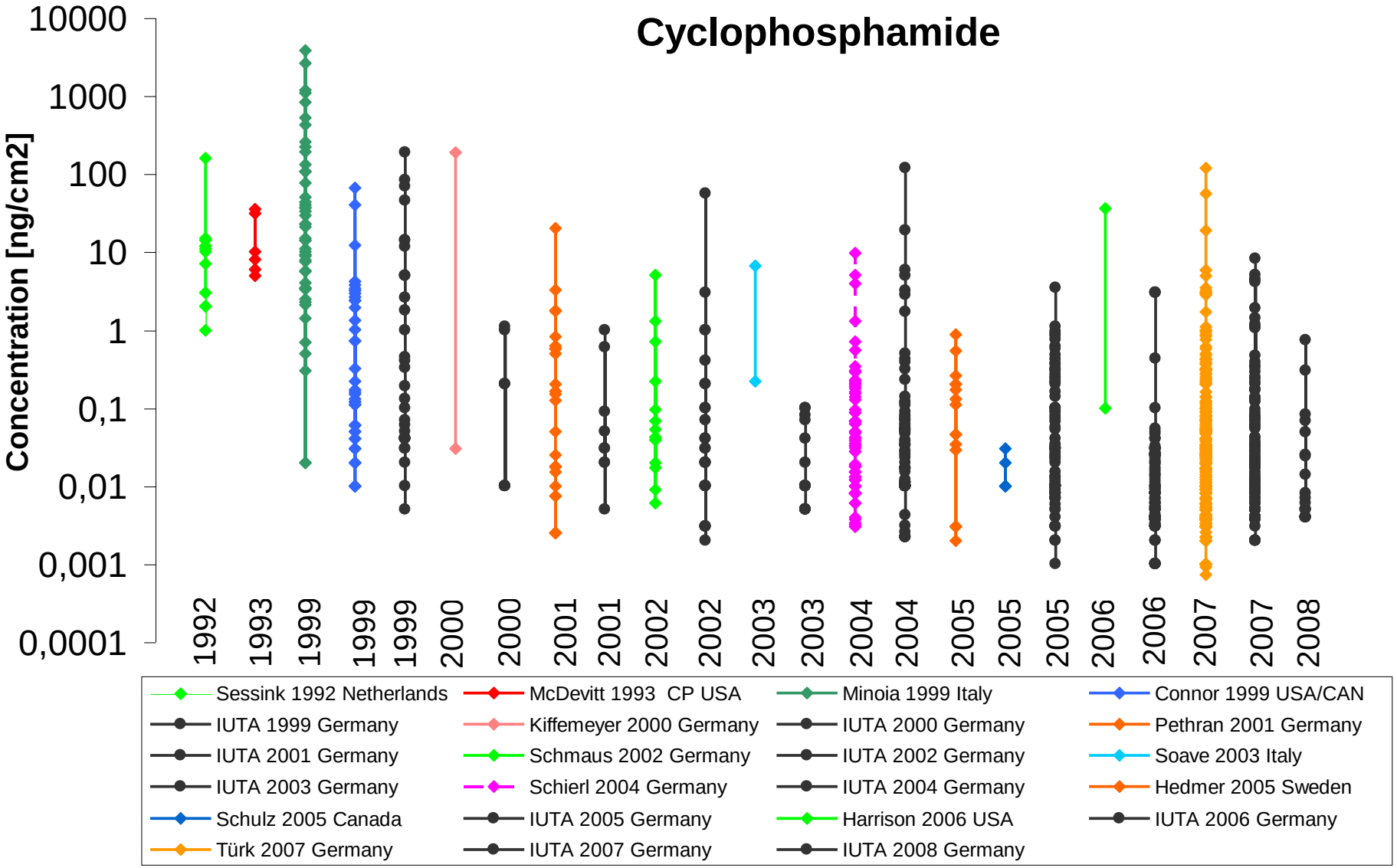
Carcinogenic effects

Reproductive effects

Assets and Drawbacks of monitoring types

	Stan-dardized	Specific for drugs	Information on causes	Information on uptake	Information on health effects	Costs
Ambient Monitoring	±	+	+	-	-	+
Bio-monitoring	±	+	-	+	±	+
Cytogenetic monitoring	+	-	-	±	±	-

Earlier Monitoring studies



The MEWIP Study

- **M**onitoring **E**ffect study of **Wi**pe sampling in **P**hamacies
- Financed by the Institution for Statutory Accident Insurance and Prevention in the Health and Welfare Services, BGW, Cologne, Germany
- From 2005-2008, Monitoring in 2006-2007
- 130 participating pharmacies
- Eight substances, three sampling spots, 2-5 cycles
- more than 1.200 samples and 10.000 measured values

Project partners

	Institution for Statutory Accident Insurance and Prevention in the Health and Welfare Services, BGW, Cologne, Germany, *Dr. André Heinemann, Dr. Udo Eickmann*	**Financing, Organization**
	Institute of Energy and Environmental Technology, IUTA, Duisburg, Germany *Dr. Thekla Kiffmeyer, Dr. Jochen Türk*	**Organization, Analysis**
	Institute of Medical Statistics, Computer Science & Epidemiology, IMSIE, Cologne, Germany *Dr. Hartmut Stützer, Dr. Moritz Hahn*	**Statistical analysis**
IfAP e.V.	Institute of Applied Pharmacy IFAP, Cologne, Germany *Pharmacist Caudia Hadtstein*	**Data collection, Organization**

Objectives of the MEWIP-Study

1. **Primary aims:**

   - **Investigate suitability and effects of a regular monitoring**
   - **Determinate the contamination level**

2. **Secondary aims:**

   - **Investigate origin and spread of contamination**
   - **Develop strategies for minimization of exposure**

Methods: Selection / allocation of participants

- More than 200 pharmacies interested, (total approx. 800 in D)
- Excluded: isolators, < 500 preparations/year, difficult to reach
- 130 randomly selected; 78 hospital, 52 public pharmacies
- Divided into 2 groups: A (55) intensive monitoring, B (75) control
  - **Group A:** 5 monitoring cycles, ≈ every 3-4 months
    receiving results during study➔ targeted actions
  - **Group B:** 2 monitoring cycles at beginning and end of the study
    no results before the end of the study

Methods: Registration of work procedures

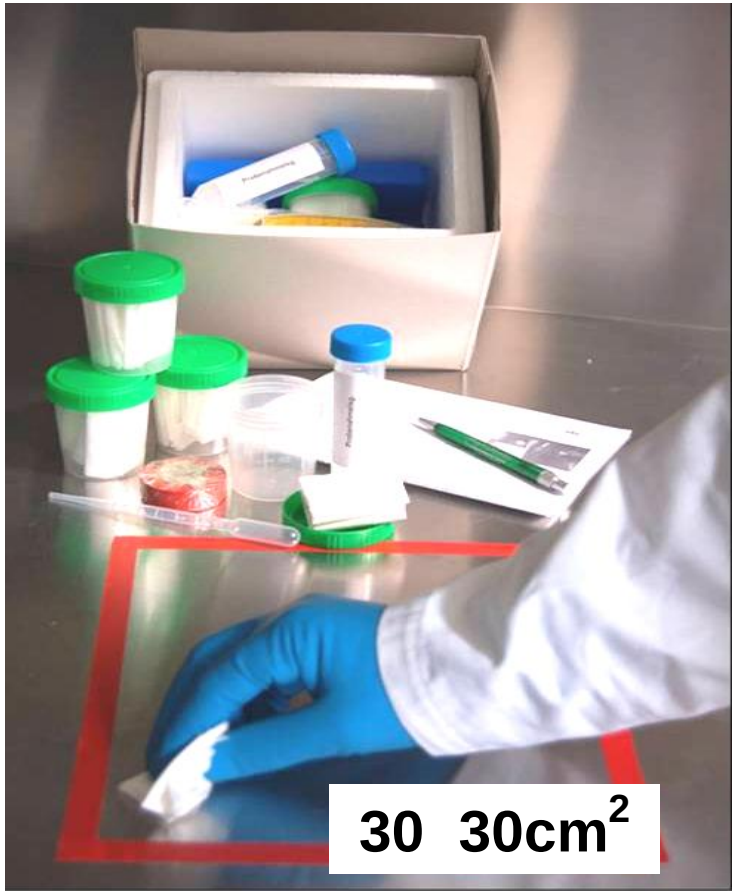
Visits in each pharmacy at the begin of the study:

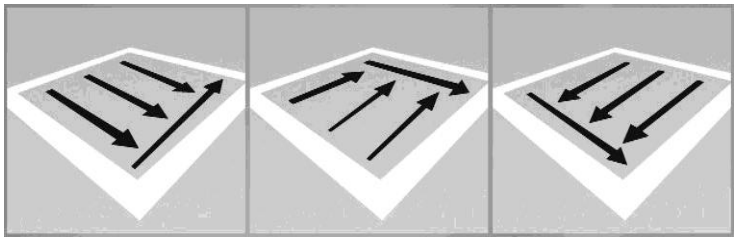
- 1. Detailed questionnaire on work procedures (12 pages)
  - a) type and amounts handled
  - b) hazards and spillage
  - c) cleaning procedures
  - d) waste management
  - e) education, tasks, working hours of personnel
  - f) protective clothing and equipment
  - g) participation in training seminars
  - i) participation in monitoring programs

2. Questionnaire for each sampling round (a, b, c and changes)

3. Feedback questionnaire after monitoring program

Methods: Sampling kit





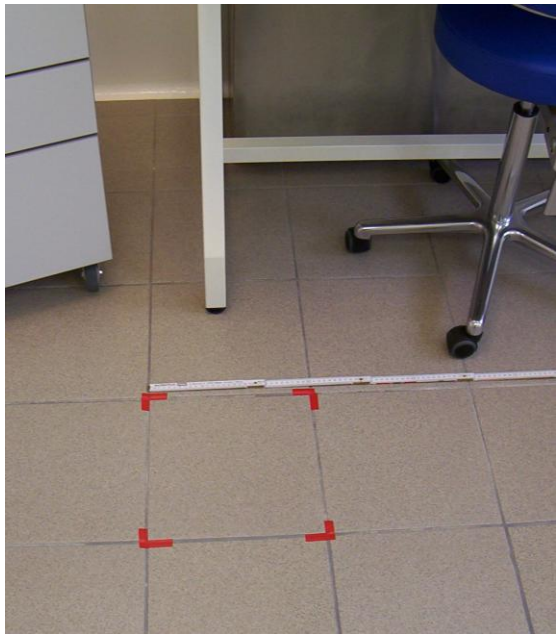
- Wipe sampling by pharmacy personnel using IUTA kit and standard operation procedure
- Demonstration and explanation during visits
- Sampling after work shift, before cleaning
- Cooled samples send in 24h to IUTA
- Sample pretreatment and analysis at IUTA laboratories

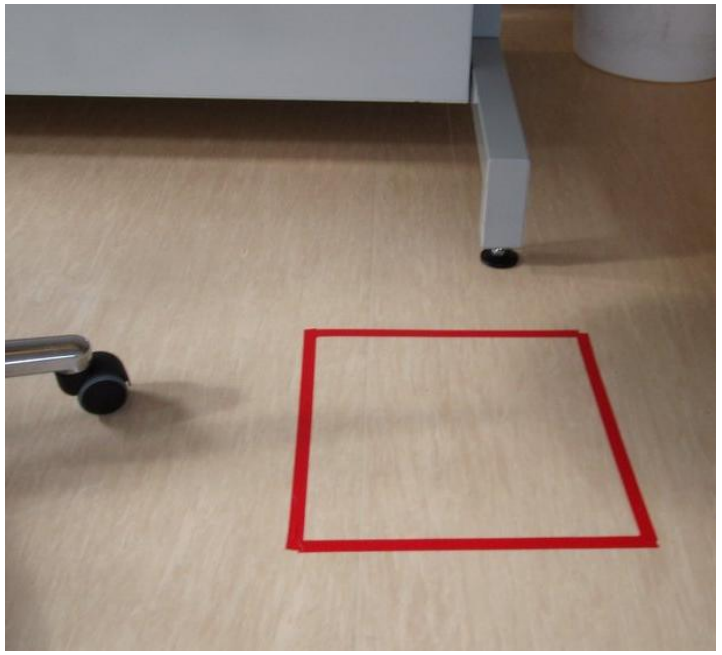
Methods: Sampling procedure

1. Make sure that the freezer packs are frozen
2. Mark area, document sampling spots (photos)
3. Label PE beaker with sample number and position
4. Spread 1 mL sampling solution on one wipe
5. Wipe sampling area in one direction
6. Repeat 5 with two more wipes in the other two directions
7. Put all wipes from one position in one labeled beaker
8. Fill in Document Form and Sample List
9. Pack samples, forms and freezer packs into the box
10. Return package to IUTA within 24h or store at -18°C

Methods: Sampling spot 1

1. Floor in front of the (most intensively used) safety cabinet

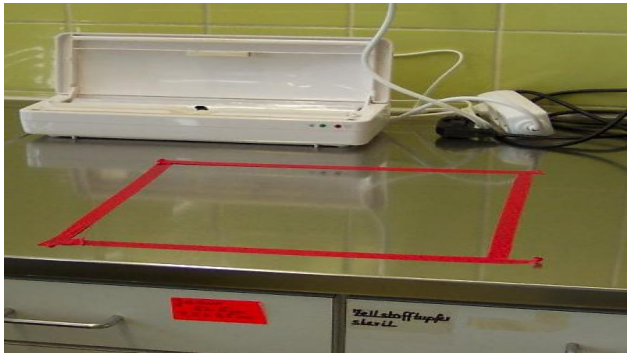




Plastic, linoleum, PVC	84,6%	Other	3,8%
Tiles	8,5%	No information	1,5%
Parquet, Laminate	1,5%		

Methods: Sampling spot 2

2. Work top (most intensively used)



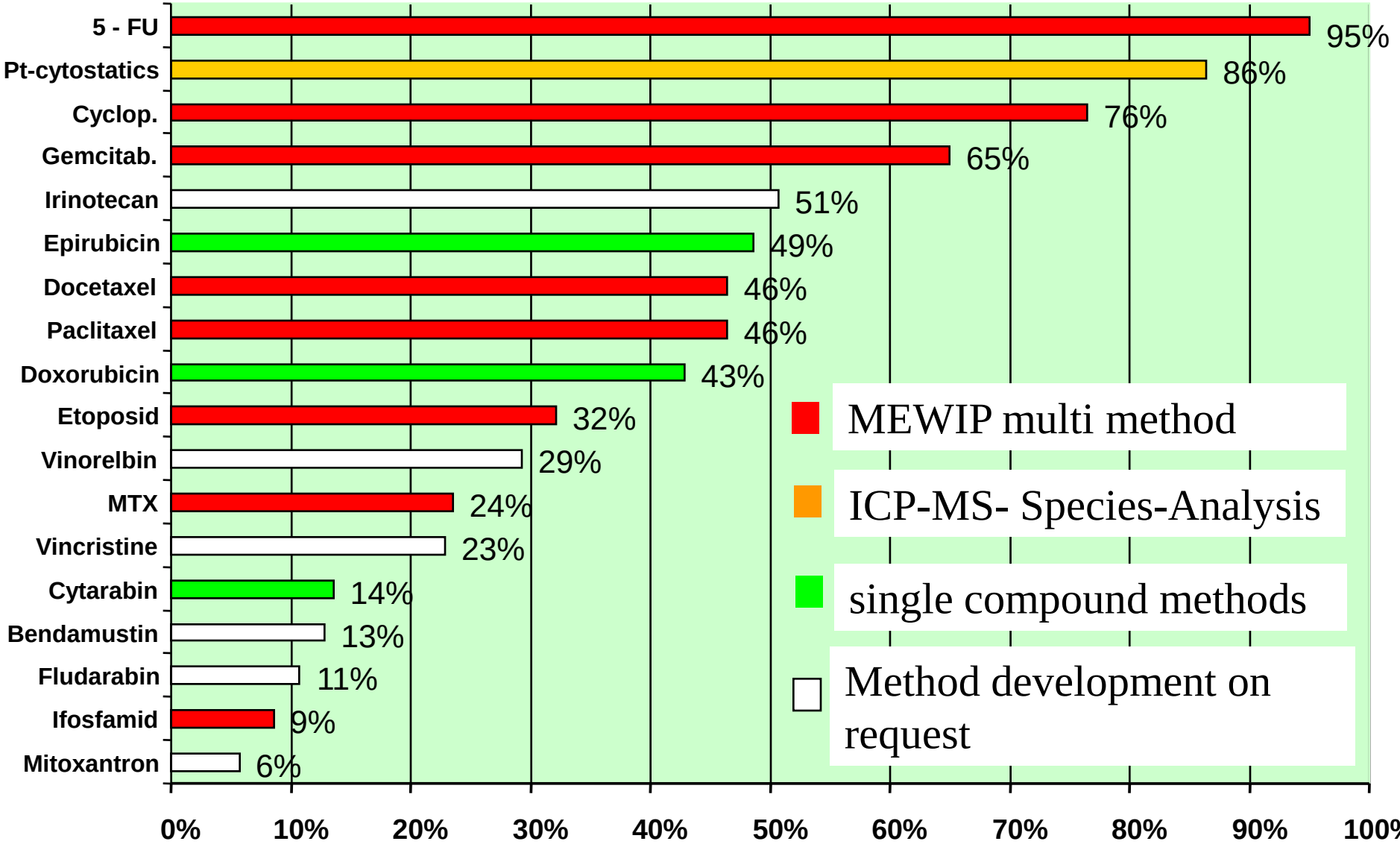
HDF chipboard	60,8%	Other	0,8%
Stainless steel	36,2%	No information	0,8%
Stoneware, ceramics	1,5%		

Methods: Sampling spot 3

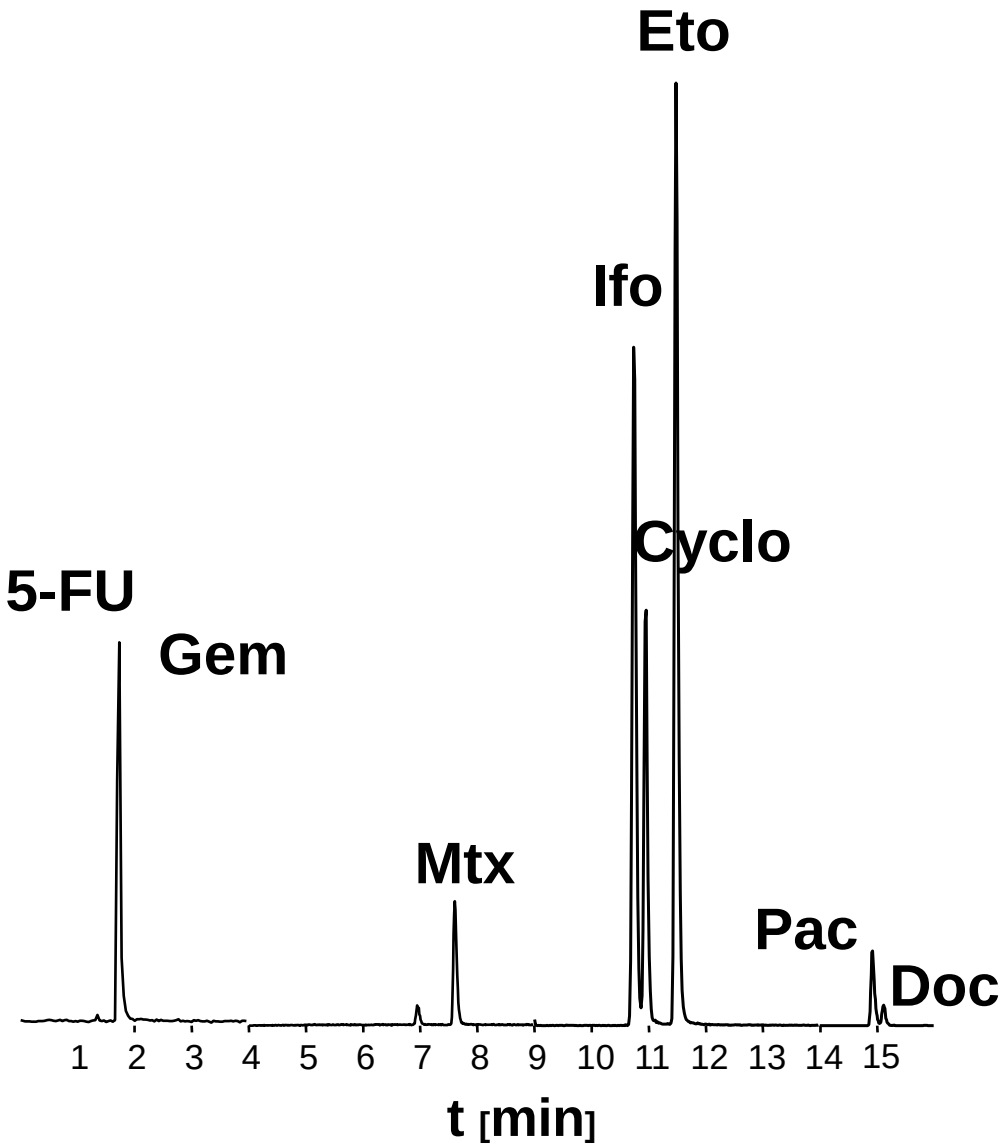
3. Fridge door including handle

Coated, painted metal	78,5	Other	10,8
HDF chipboard	4,6	No information	1,5
Glass	4,6		

Methods: Compounds



Methods: HPLC-MS/MS multi method

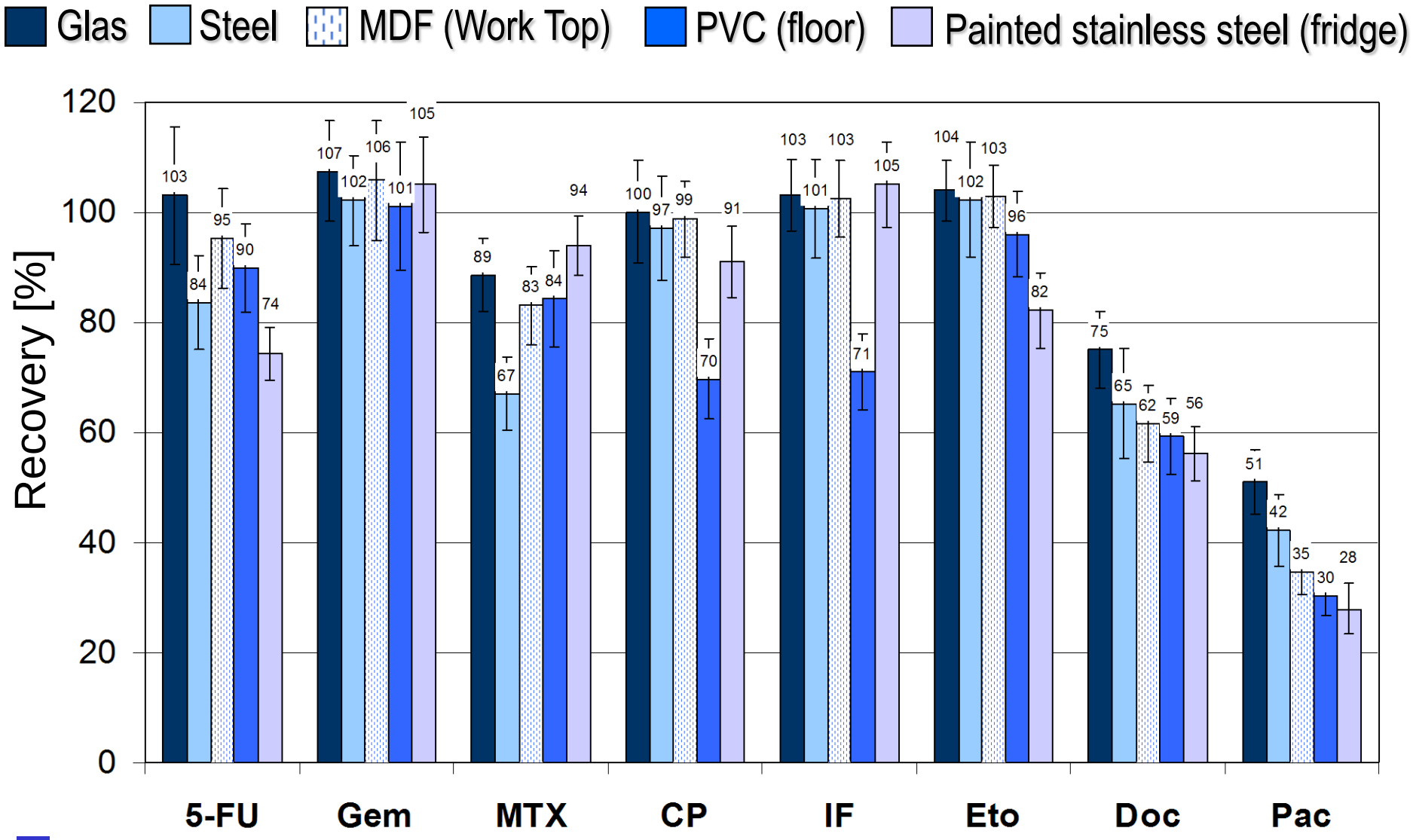


Matrix standard: c = 50ng/mL 50x3mm
Shim-Pack XR-ODS, 2,2µm column
T = 30°C, Flow: 300µL/min
Ionisation: Electrospray (ESI)
1. Period: 0–4min, 2. Period: 4–9min,
3. Period: 9–14min,
4. Period: 14–16min.
Gradient: 0-1min 95% A, 15min 50% A,
20 min 50% A, 21 min 95% A,
25 min 95% A
A: 0,1% Formic acid in water,
B: 0,1% Formic acid in ACN

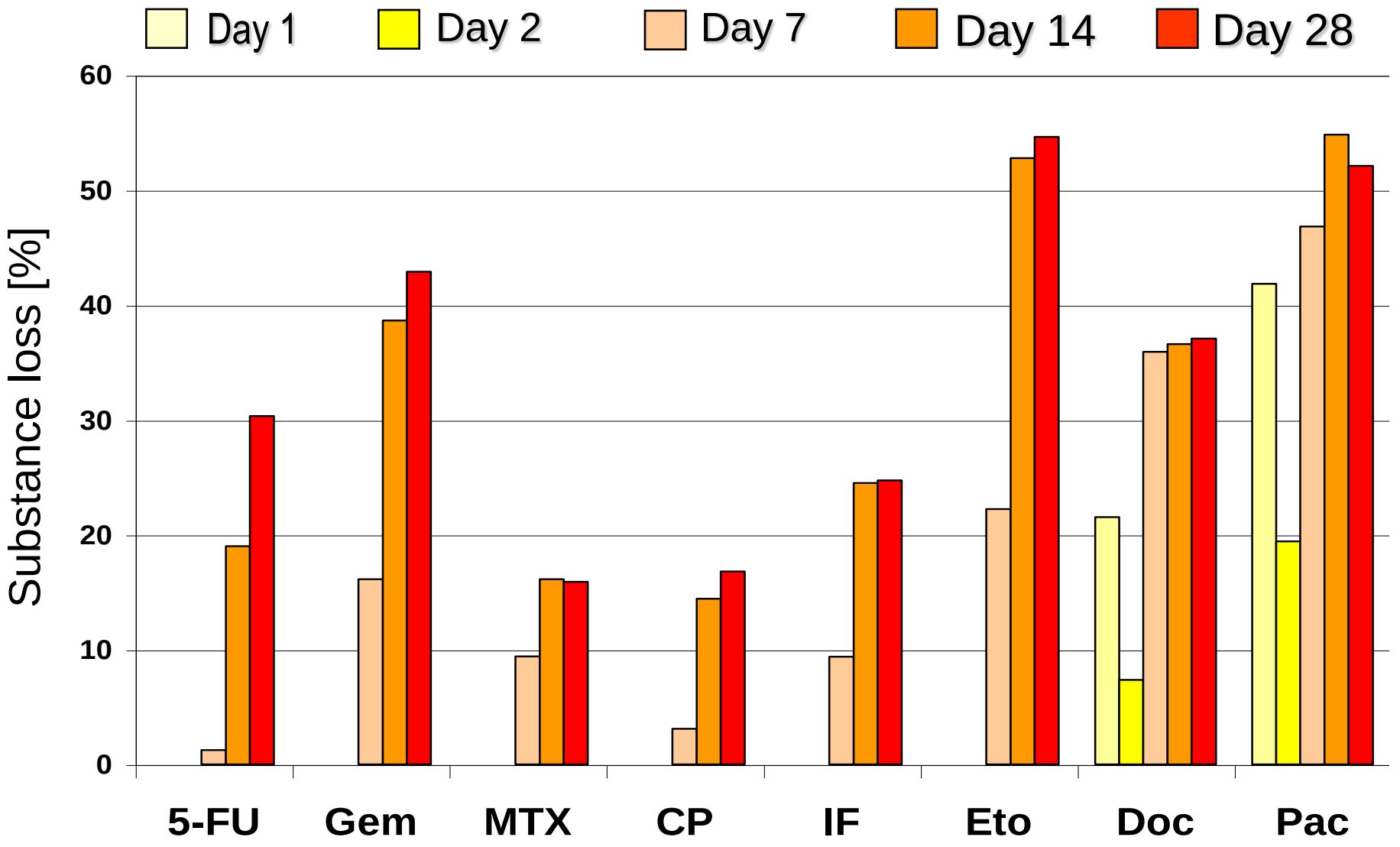
LODs [ng/cm^{2}]:

5-FU:	**0.011**	**Eto:**	**0.0073**
Gem:	**0.0073**	**Cyclo:**	**0.0037**
MTX:	**0.0037**	**Pac:**	**0.0367**
Ifo:	**0.0037**	**Doc:**	**0.0183**

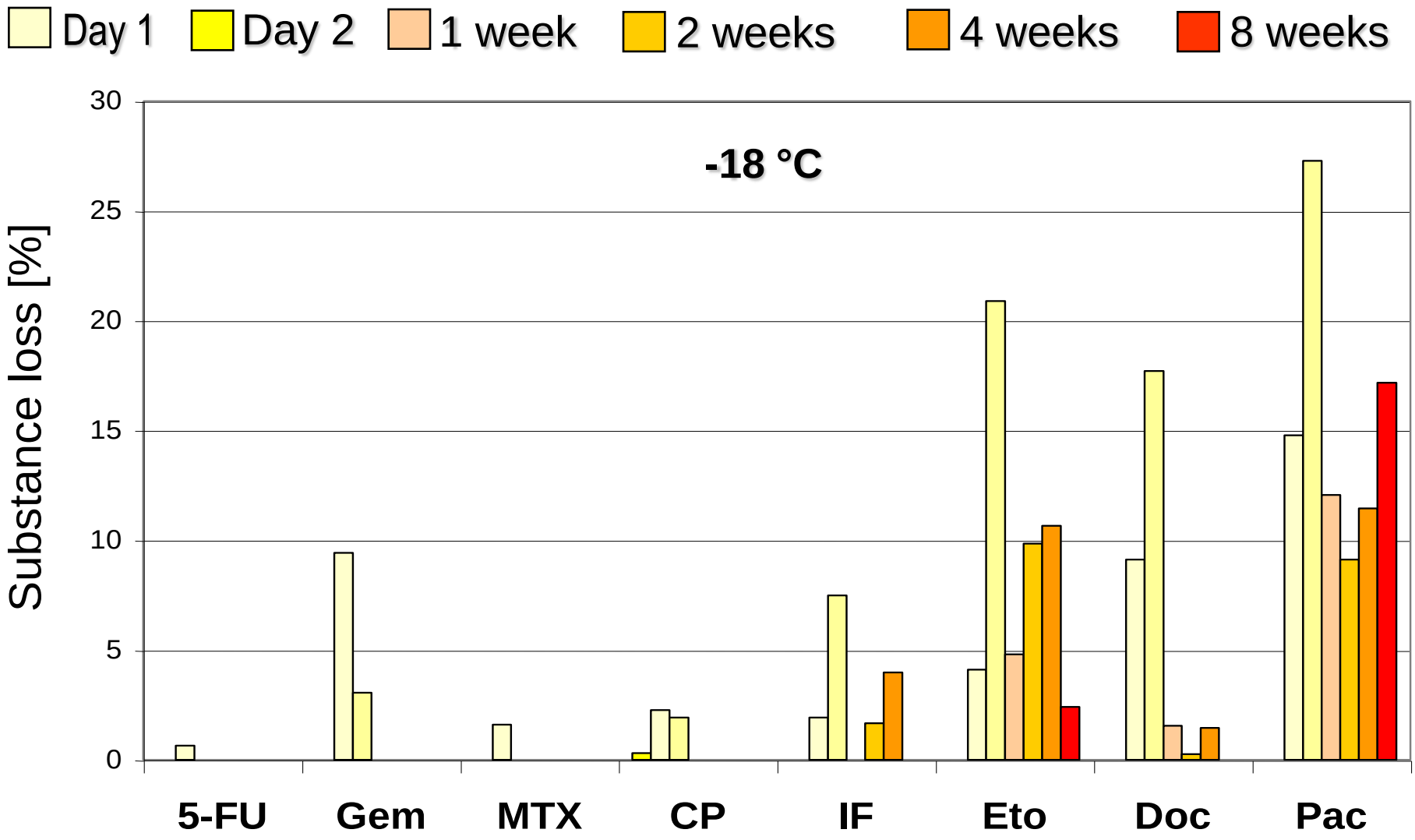
Validation: Influence of surface material



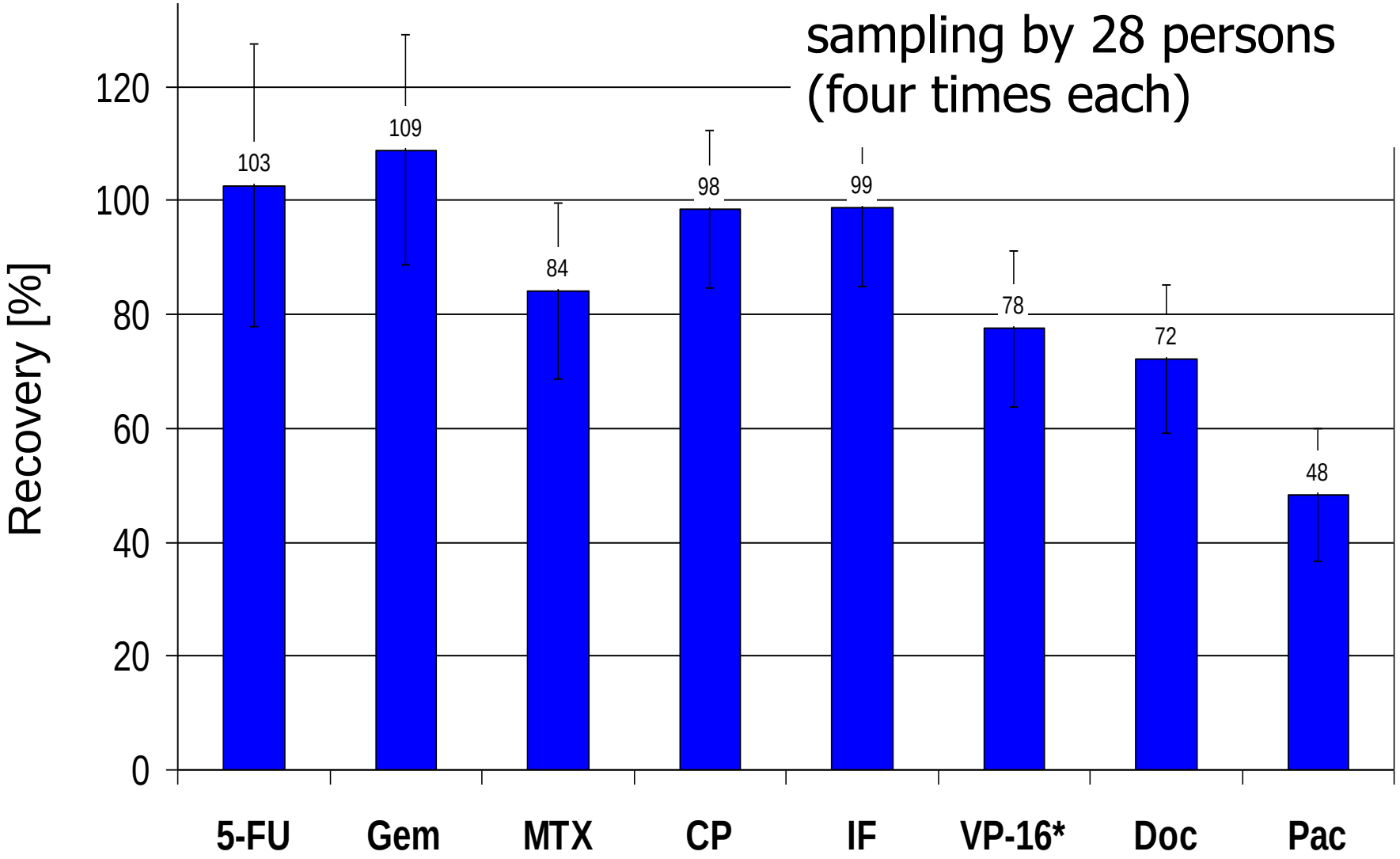
Validation: Influence of sample transport



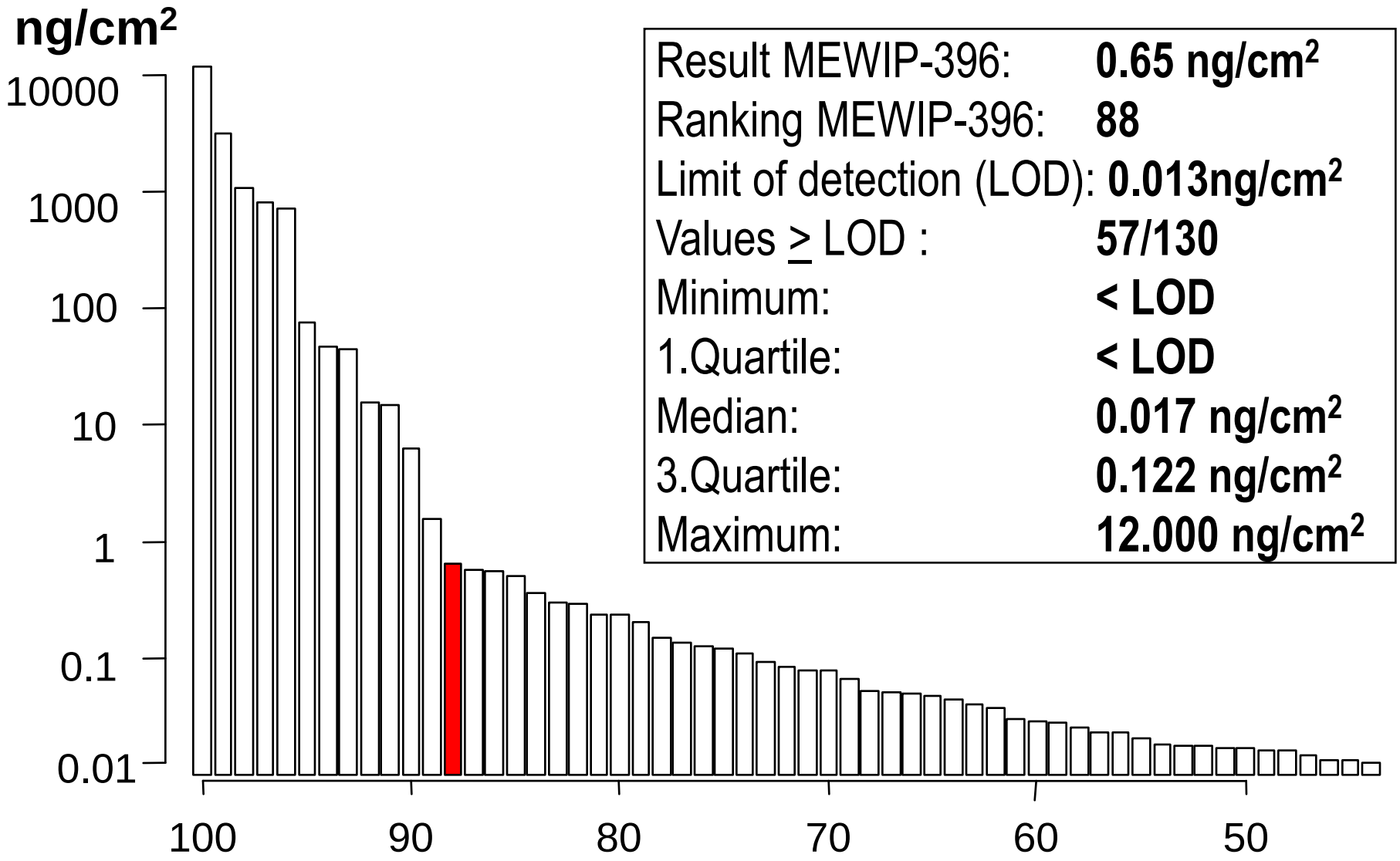
Validation: Influence of sample storage



Validation: Influence of sampling person

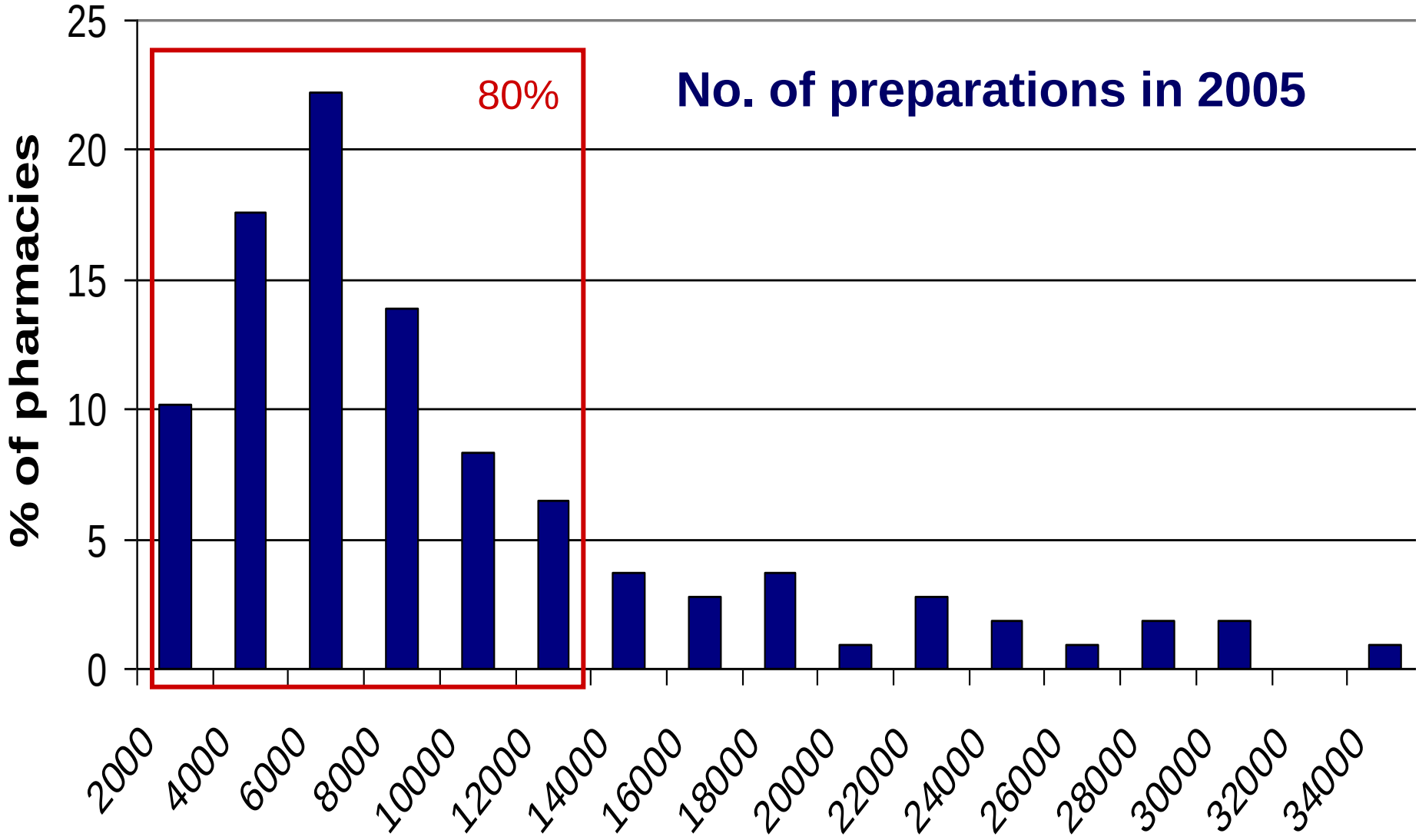


Methods: Reports for participants

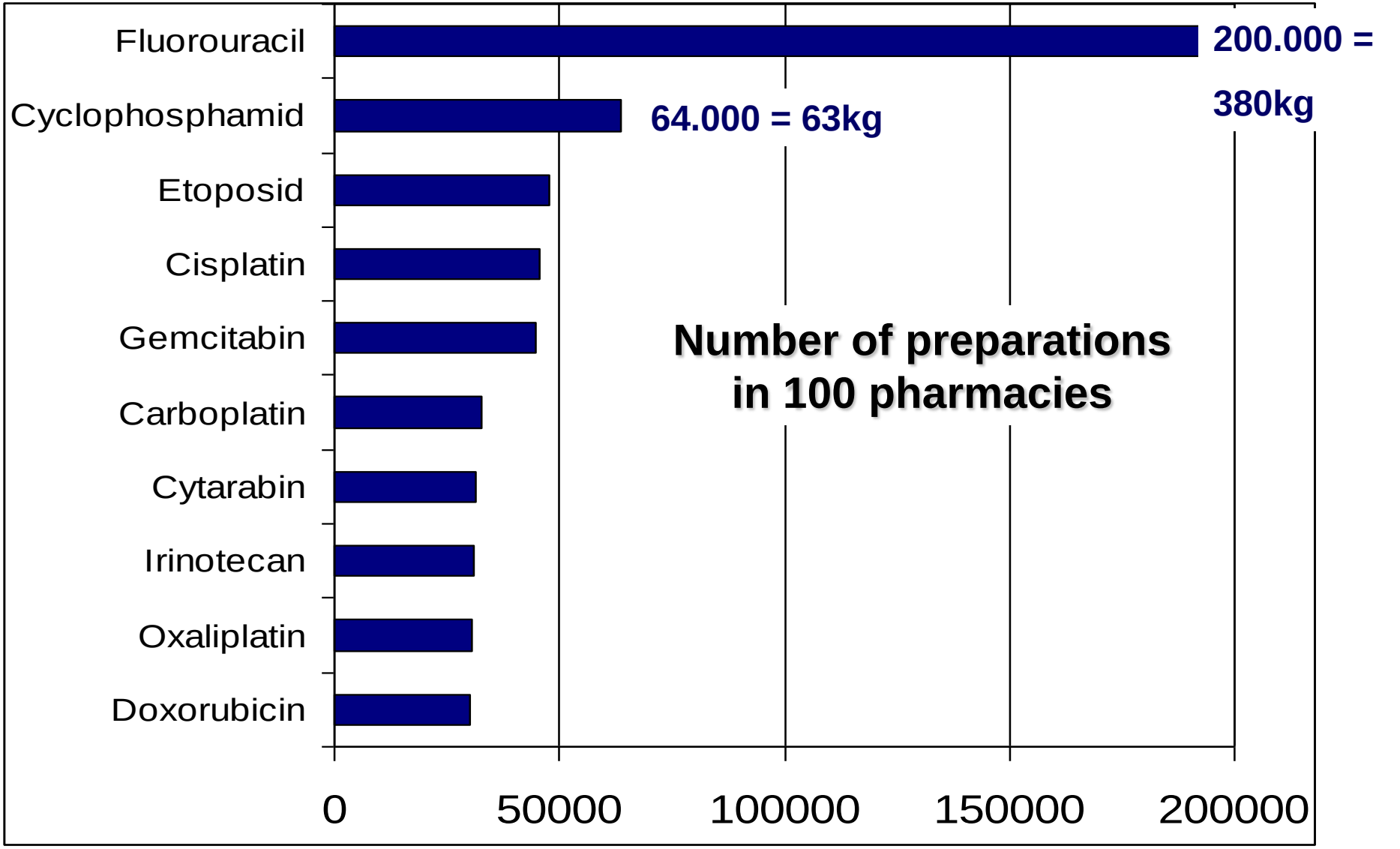


Result MEWIP-396:	**0.65 ng/cm²**
Ranking MEWIP-396:	**88**
Limit of detection (LOD):	**0.013ng/cm²**
Values ≥ LOD :	**57/130**
Minimum:	**< LOD**
1.Quartile:	**< LOD**
Median:	**0.017 ng/cm²**
3.Quartile:	**0.122 ng/cm²**
Maximum:	**12.000 ng/cm²**

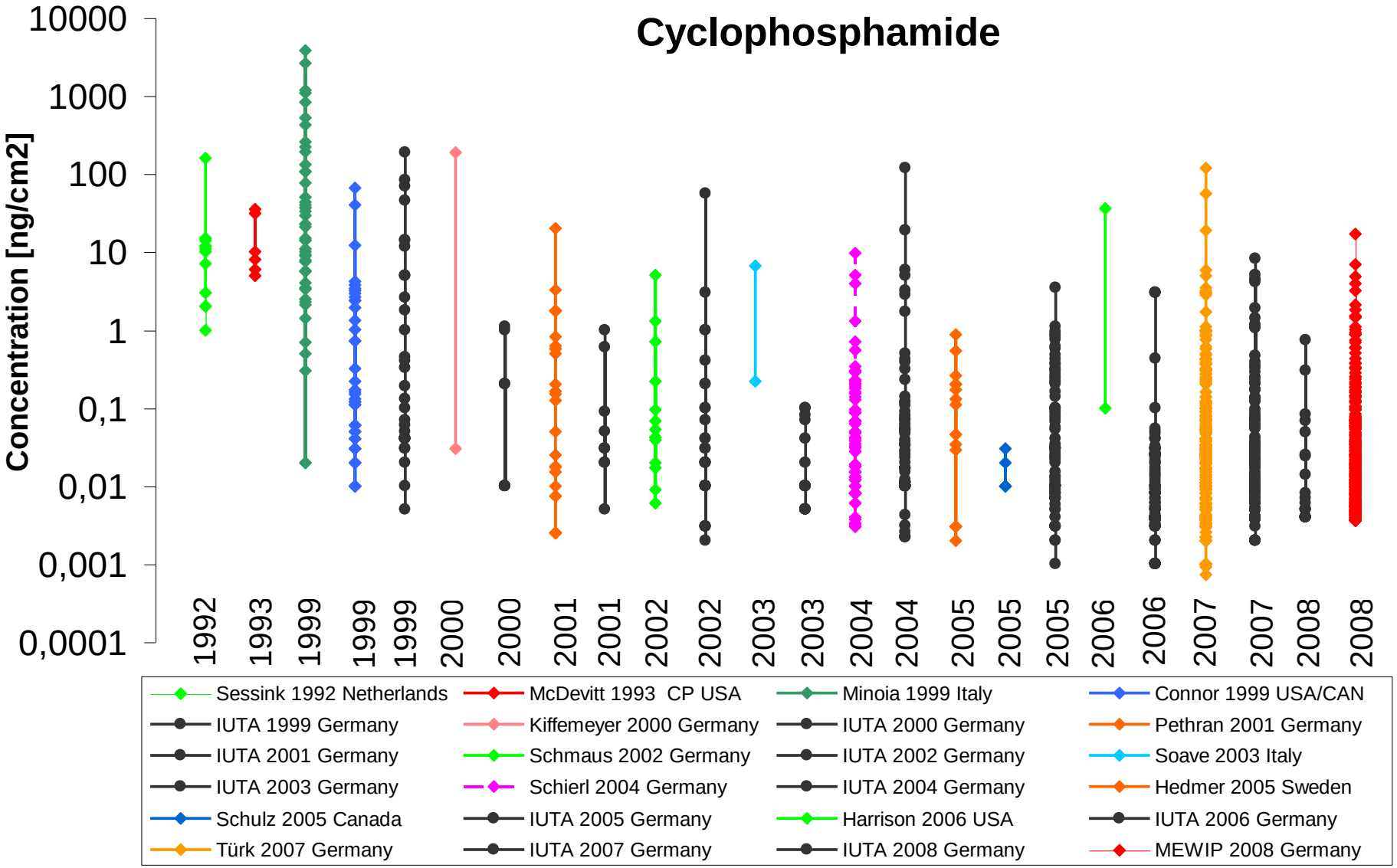
Results: Work practice



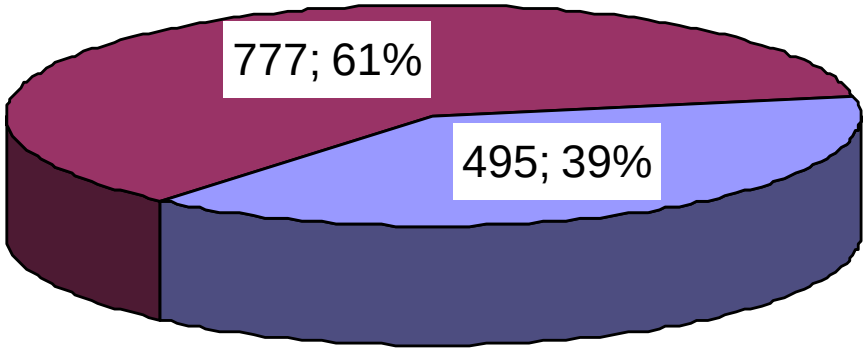
Results: Work practice

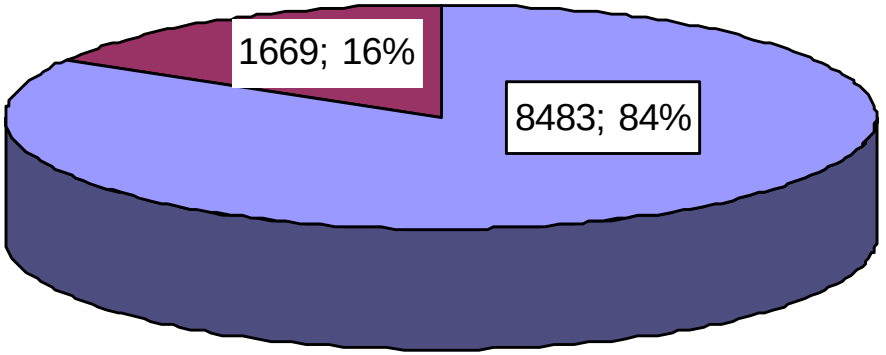


Results: Comparison with other studies



Results: Total





1.272 wipe samples

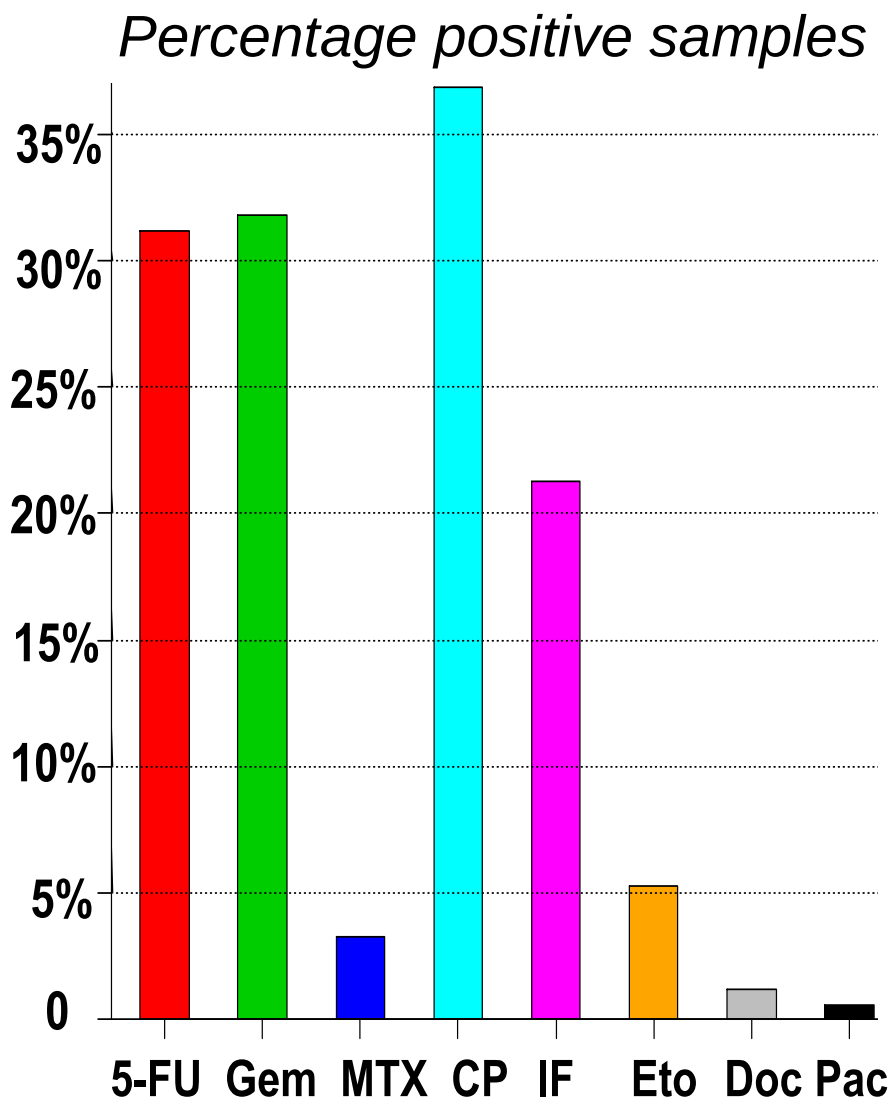
61% positive with at least one substance

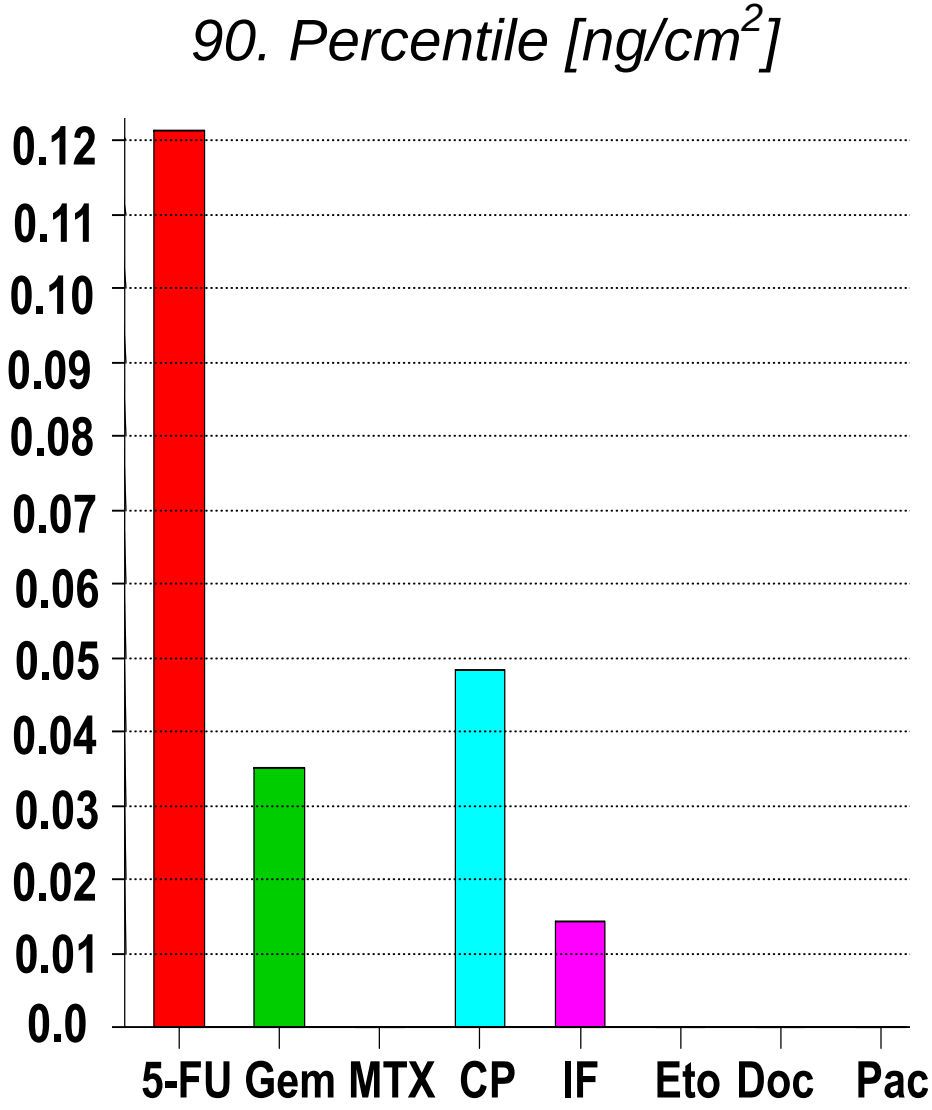
10.176 measurements

16% positive for the single compound

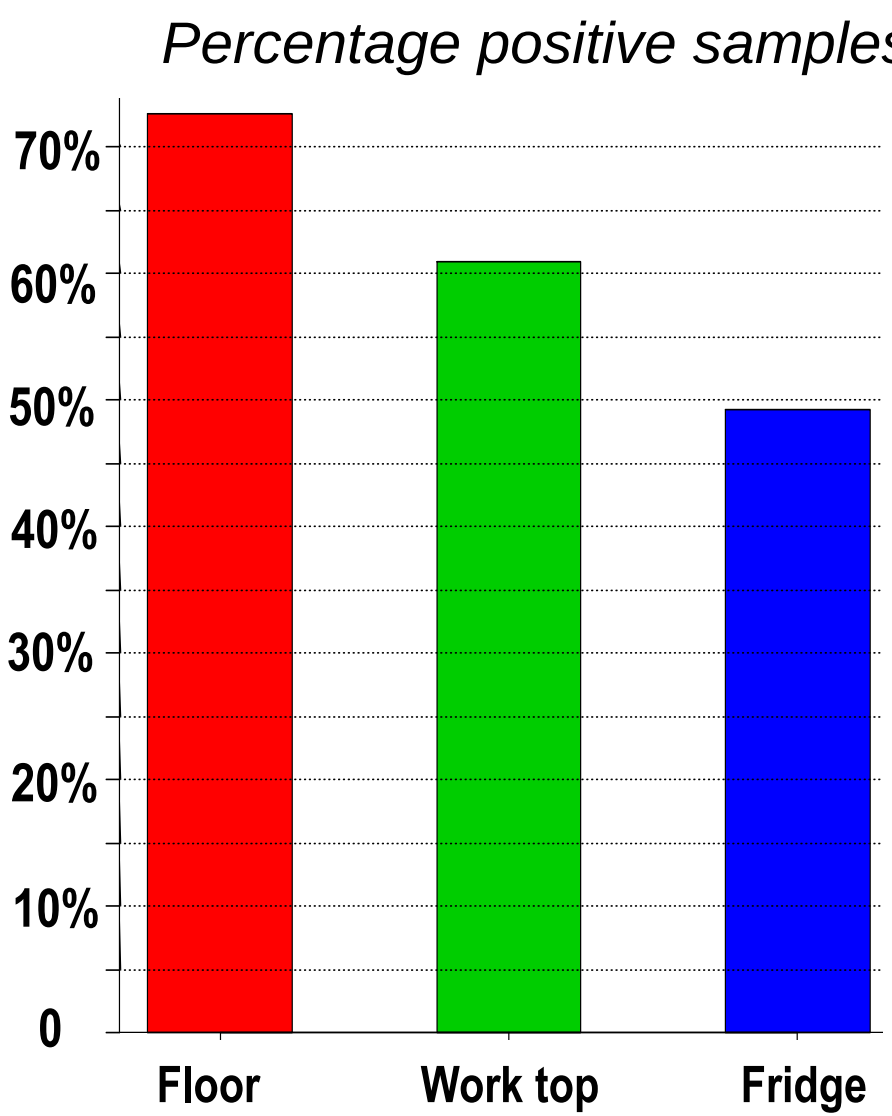
Average area contamination	2.909 ng/cm²
Total contamination	2.618.273 ng

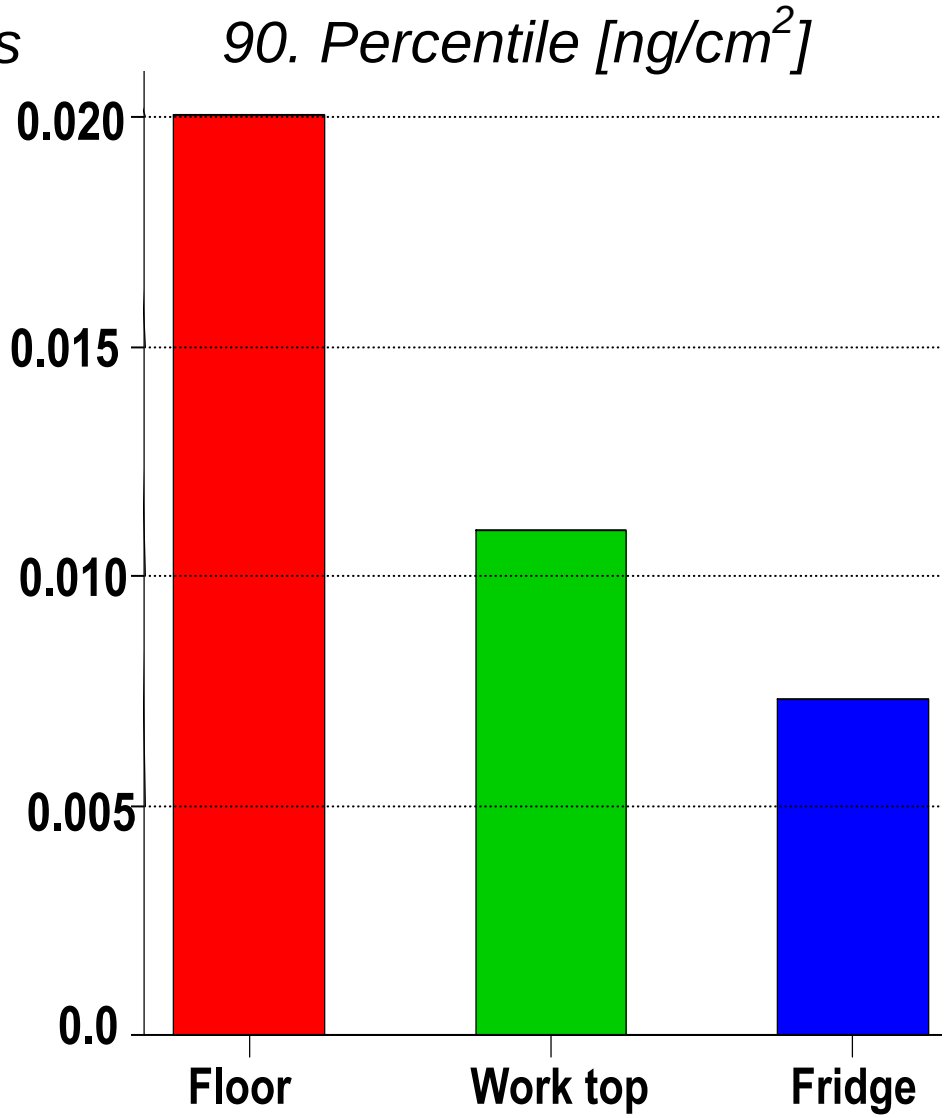
Results: Eight substances





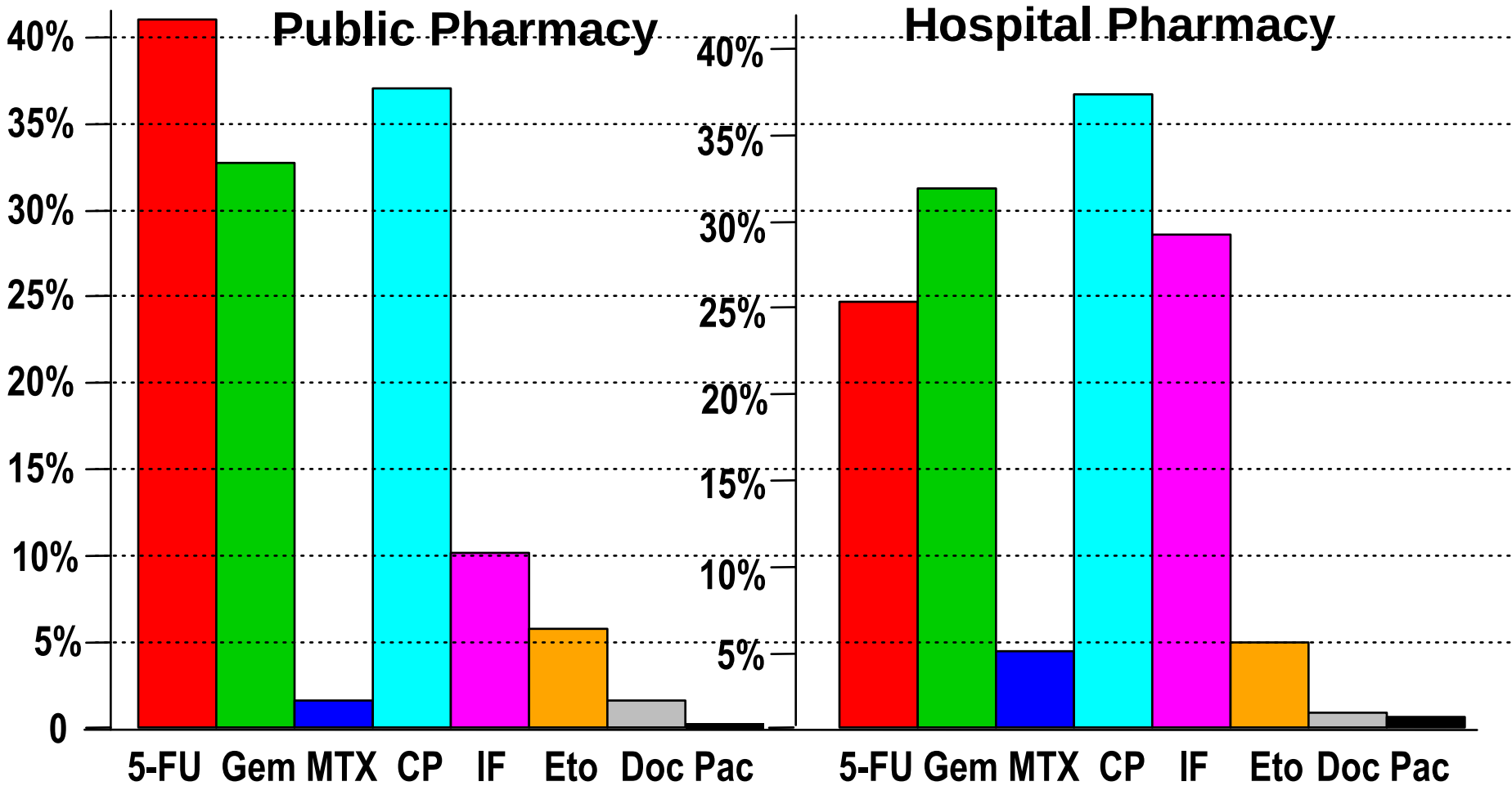
Results: Three Sampling spots



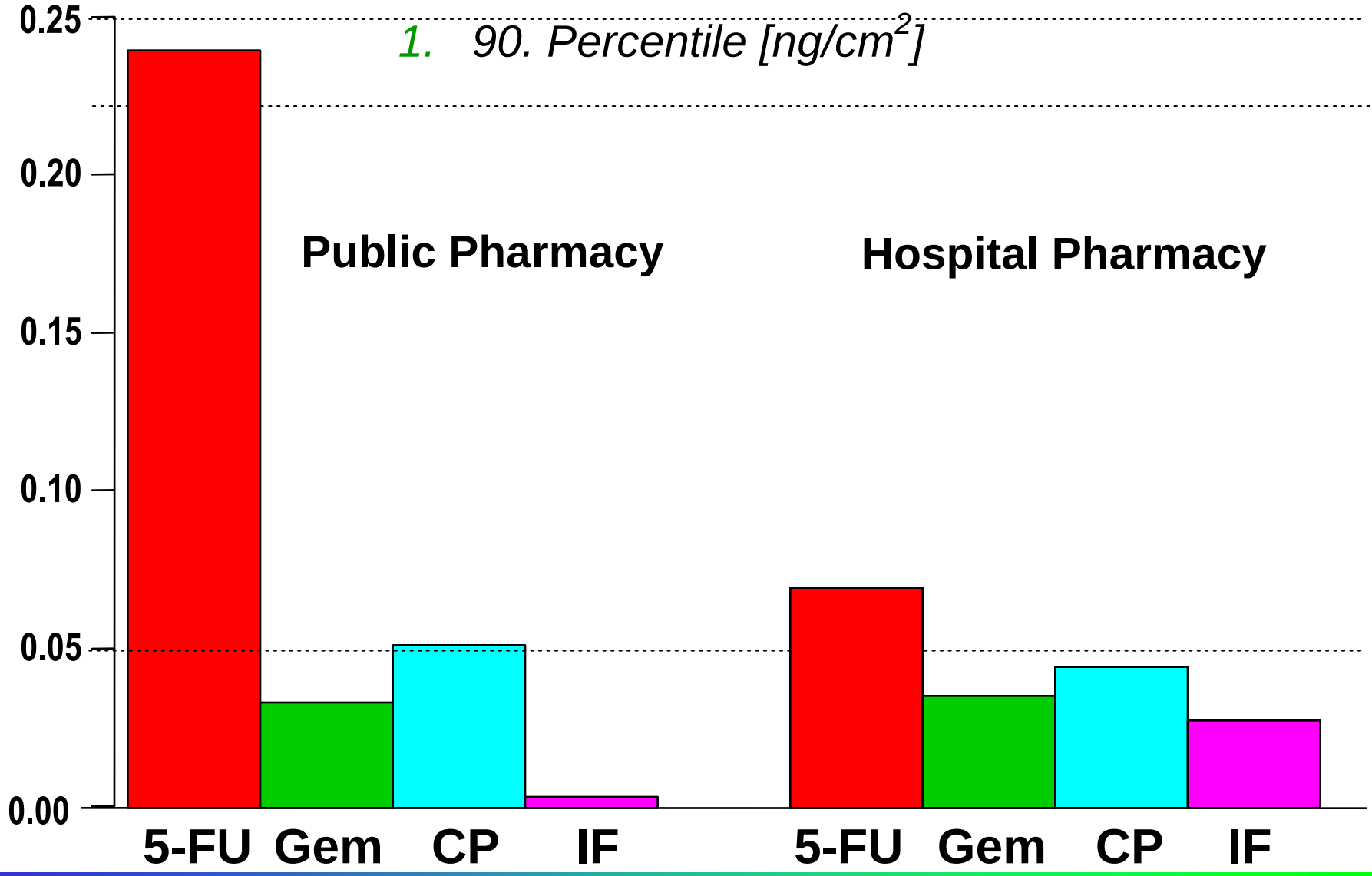


Results: Two types of pharmacies

1. *Percentage positive samples:*

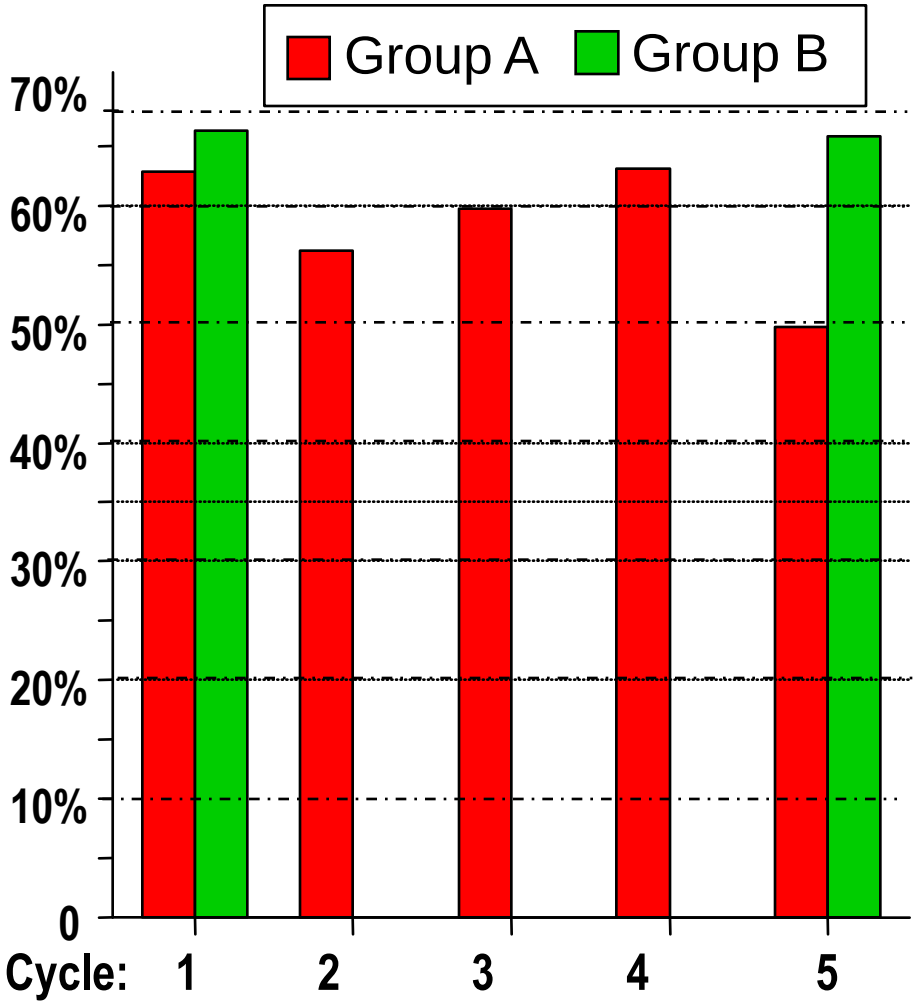


Results: Two types of pharmacies

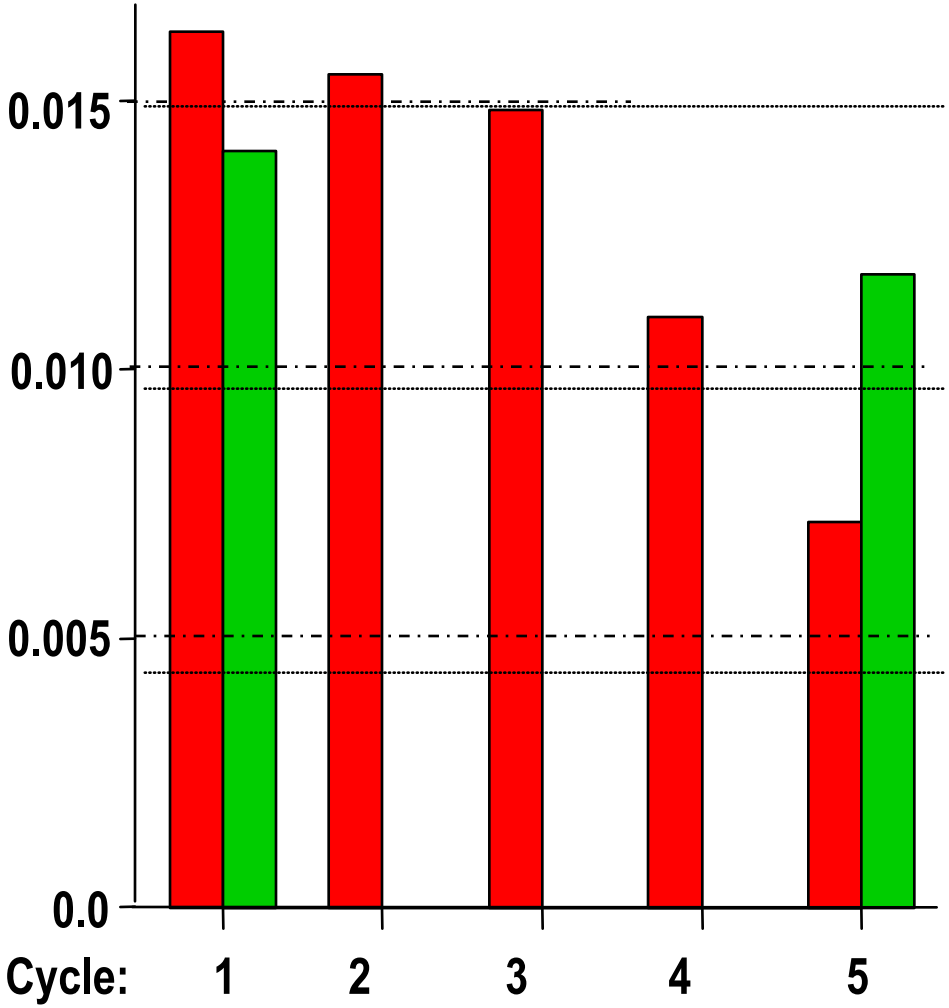


Results: Two groups; Five cycles

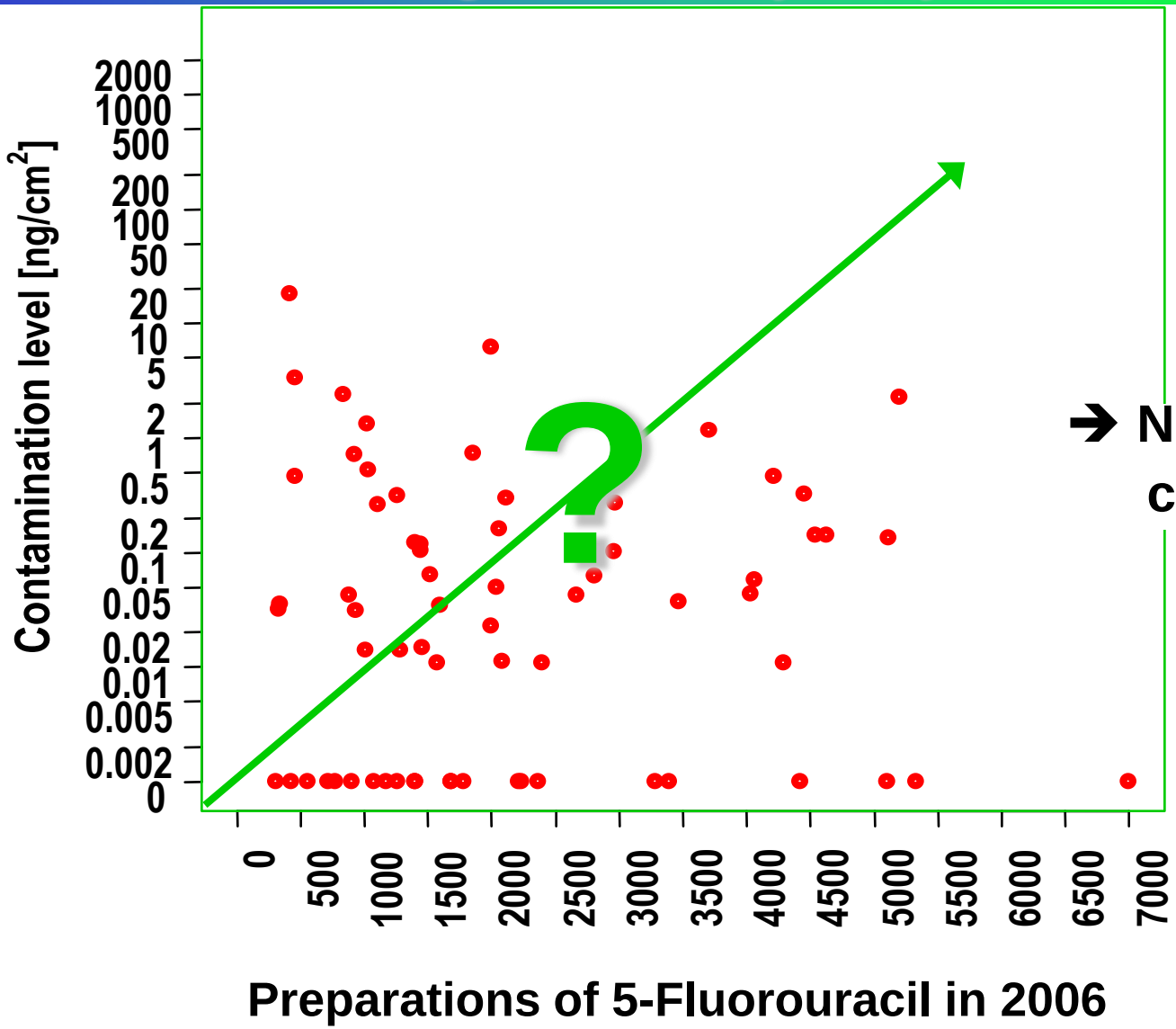
Percentage positive samples



90. Percentile [ng/cm²]

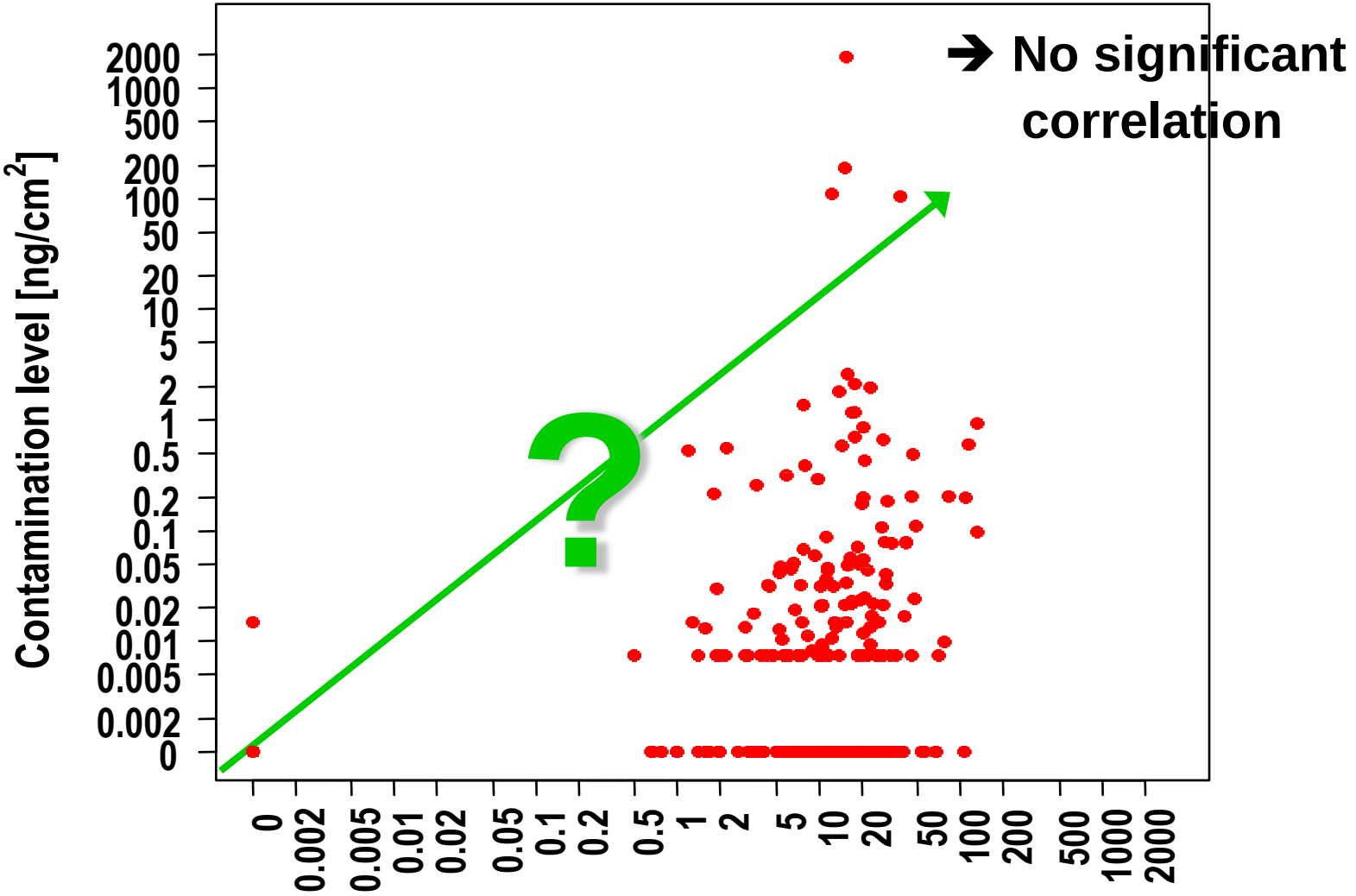


Results: Influencing factors - yearly amounts

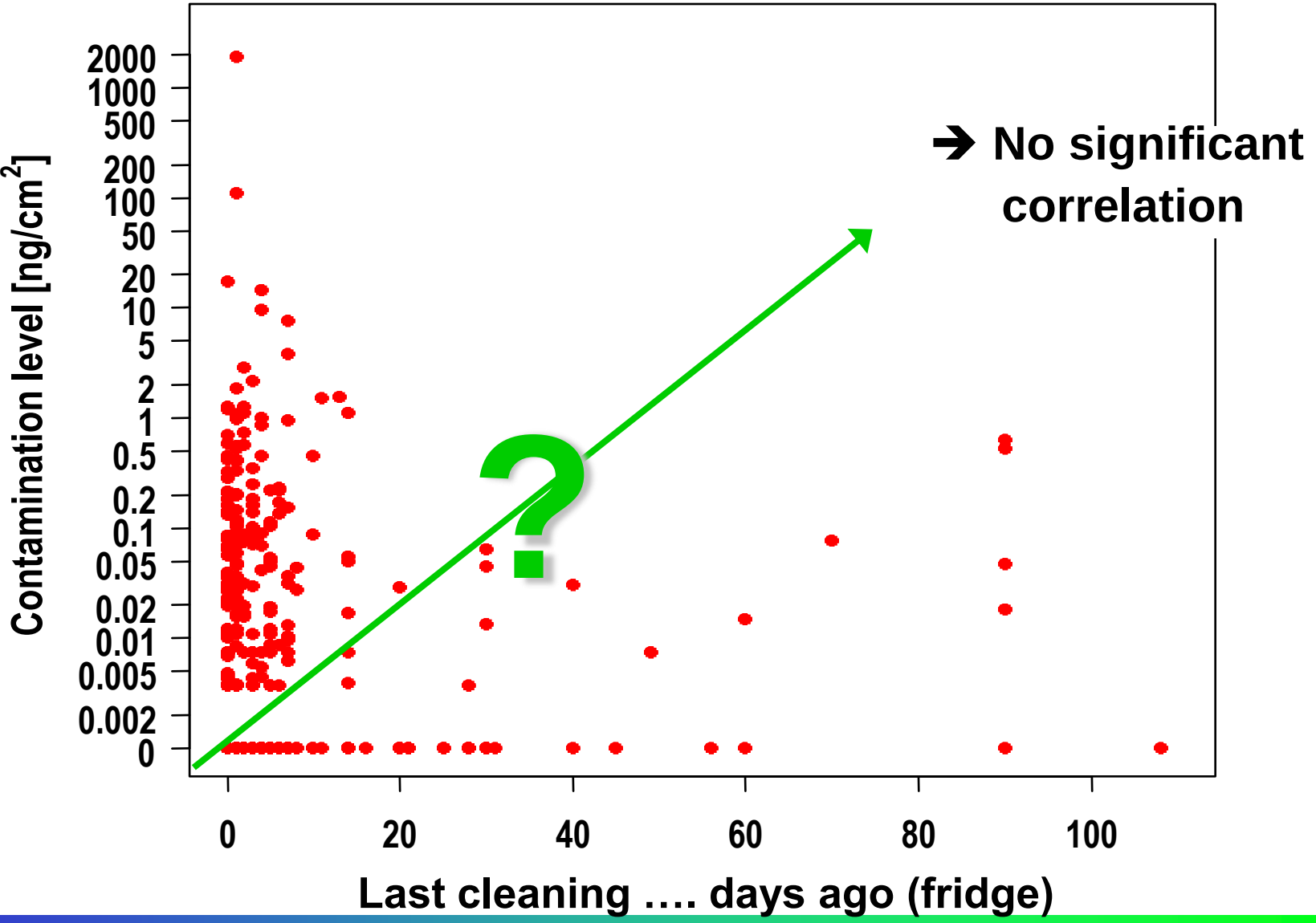


➔ No significant correlation

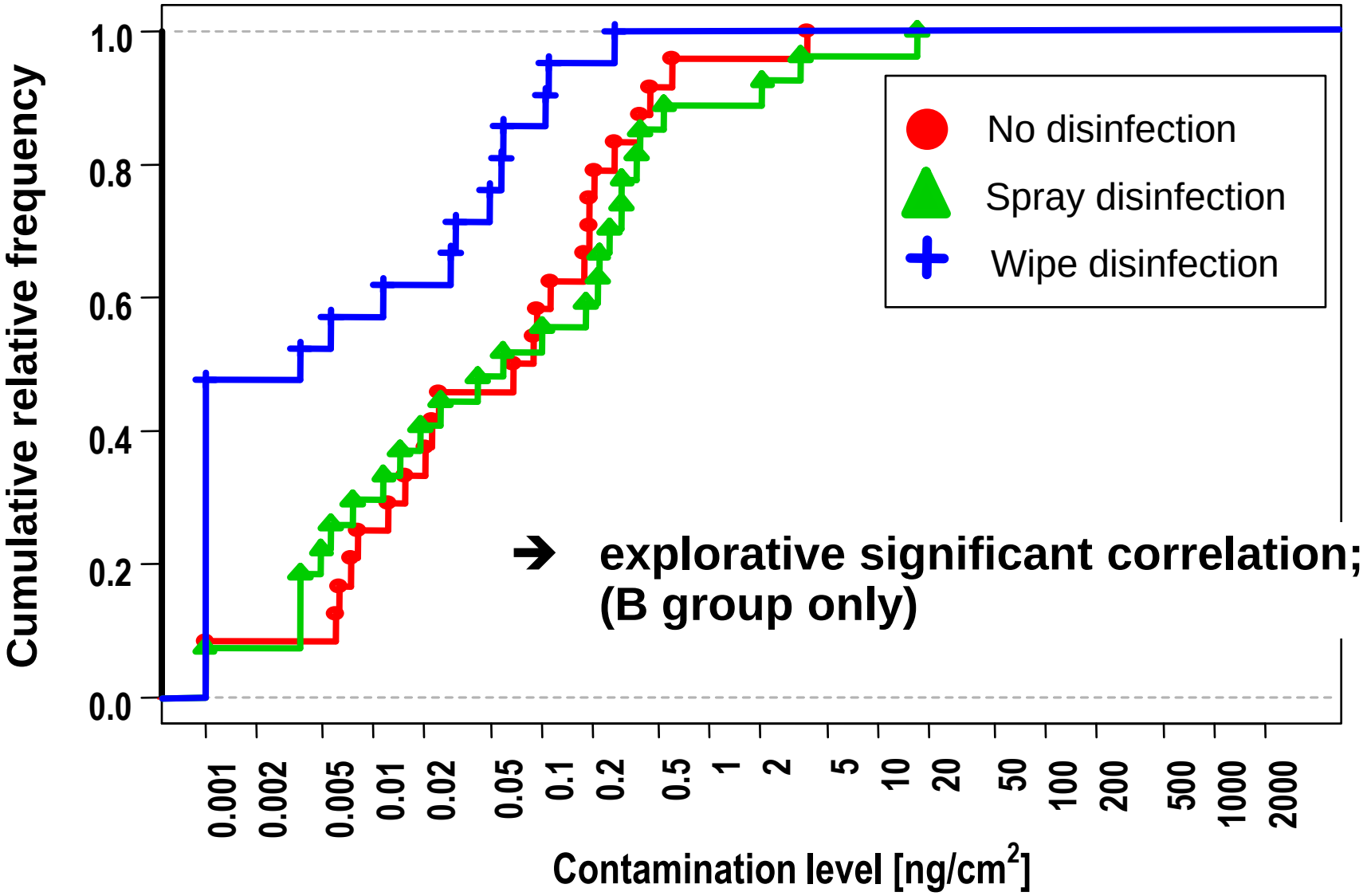
Results: Influencing factors - 5 days amounts



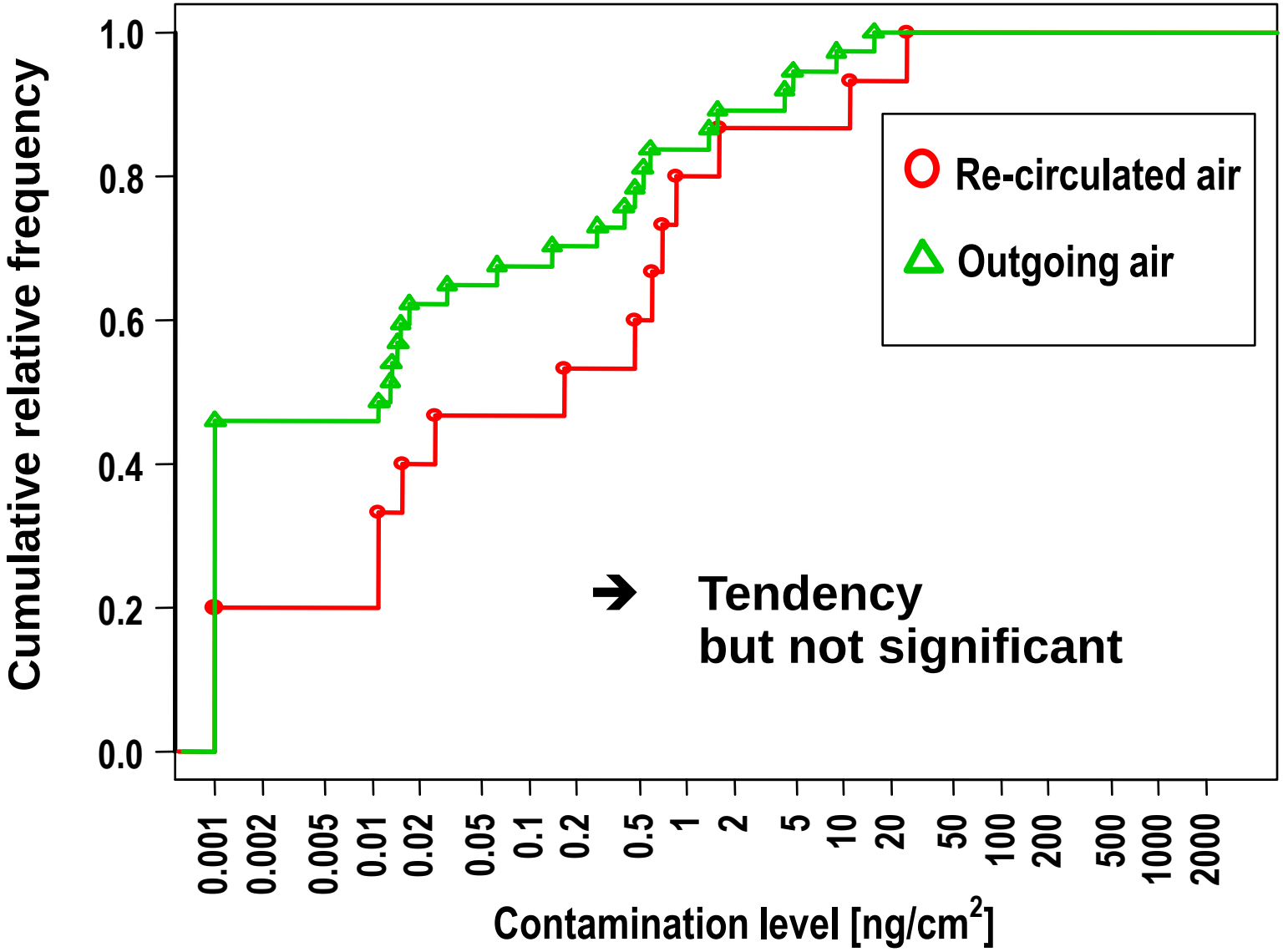
Results: Influencing factors - cleaning



Results: Influencing factors - disinfection



Results: Influencing factors - outgoing air



Consequences: In pharmacies

Examples from feedback questionnaire

1. Realised consequences:

- *"work procedures checked"*
- *"cleaning measures adapted"*
- *"change of gloves when entering storage area"*
- *"more careful working and more thorough cleaning"*
- *"additional pads used in work area"*

2. Planned consequences:

- *"revision of hygiene plan"*
- *"regular / more frequently monitoring"*
- *"cleaning and disinfection of primary packing on single use pads"*
- *"change of gloves more frequently"*

Consequences: Scientific / Political

- Regular monitoring as tool for occupational safety
- Implementation in recommendations and guidelines
- Discussion / stipulation of threshold / trigger values
- Application for other cmr drugs and compounds
- Follow up studies ambient monitoring
- Follow up studies biological monitoring
- Standardisation of Monitoring procedures
- Identification and transfer of best practise
- Harmonisation of guidelines on European level

Cleaning procedures: Surfaces

Problem:

Release is not (completely) avoidable ➔ Many surfaces are contaminated

> Safety cabinets, storage area, disposal area, floors, work tops, transport devices, furniture, working material, …

Common cleaning procedures are optimized under hygienic aspects ➔ Residues of the substances remain and are spread

➔ Cleaning procedures have to be adapted and controlled

Cleaning procedures: Surfaces

Recommendations:

- Check of cleaning procedures, detergents, intervals
- Two step procedure: 1. 0,01M NaOH; 2. ≥70% Isopropanol
- Repeat cleaning procedures several times
- Don´t use the same cleaning clothes for several rooms
- Use disposable pads or sheets
- Use removable, easy to clean containers or boxes for storage
- Wear protective clothing all the time, esp. during cleaning

Cleaning procedures: Textiles

Problem:

Textiles can be contaminated during preparation and application tasks

> Work, protective and private clothing, cleaning clothes, bed linen, patient clothes, …

Common cleaning procedures are optimized under hygienic aspects ➔ Residues of the substances remain and are spread (other clothes, waste water)

➔ Cleaning procedures have to be adapted and controlled

Cleaning procedures: Textiles

Recommendations:

- Be aware of potential contamination of textiles
- Keep textiles separated and labeled
- Wash textiles separately as infectious laundry
- Use disposable work clothes
- Wear protective clothing when handling laundry

Cleaning procedures: Vials

Problem:

Most of the vials are delivered with external contamination

- During filling ➔ low but widespread contamination
- Breakage during transport ➔ rare but high contamination

Also Infusion bags, applications,

➔ Cleaning procedures of manufacturers have to be improved

Cleaning procedures: Vials

Recommendations:

- Be aware of external contamination
- Two step cleaning procedure: 1. 0,01M NaOH;
  2. ≥70% Isopropanol
- Use vials with additional coating
- Ask supplier for control and counter measures
- Wear protective clothing all the time esp. during unpacking

Spill management: Definition

(Severe) accidental release outside the safety cabinet

= immediate removal is not possible

➔ Measures have to be established in advance

➔ Regular training is required

Criteria:

- Persons contaminated?
- Amounts, concentration
- Liquids, solids
- Place of contamination

Spill management: Spill kit

➔ **Commercial products or self assembled equipment**

Useful compounds:

- Instruction, list of contents, best-before-date
- Sufficient and fitting protective clothes and equipment
- Marking material
- Plastic or cardboard and dustpan to remove sharps
- Sufficient absorbing pads, wipes, paper
- Labeled plastic bags for waste
- Report form(s)

Spill management: Order of measures

0. Keep calm!!!
1. Get help
2. Help persons
3. Put on protective clothing
4. Mark contaminated areas
5. Clean contaminated surfaces
6. Dispose of contaminated material
7. Write report
8. Medical examination, urin samples
9. Special cleaning
10. Ambient and/or biomonitoring
11. Analyse and improve spill management

Spill management: Get help

- At least one more person (protective clothing!)
- Inform superiors, colleagues, patients
- Remove uninvolved persons
- Secure contaminated areas with warning signs, cordons etc.

Spill management: Help persons

- Rinse eyes, mucous membranes and wounds with water or saline solution (min. 10 min.)
- Remove and dispose of contaminated clothes
- Rinse skin extensively, if necessary take shower
- Consult doctor!

Spill management: Protective clothing

- Gloves, gown/Overall, cuffs, overshoes, respirator mask, goggles
- Should cover the whole body esp. legs and shoes
- Should fit, not hinder or spread contamination
- Should be sufficient for at least two persons

Spill management: Mark contaminated areas

- Record puddles, splashes, residues of solids
  - Marker, chalk etc.
  - Tape or rope
  - Paper towels
  - Record through colleagues
  - Photos

➔ Leave marks for final cleaning and control monitoring

Spill management: Cleaning

- From outside to inside
- Careful remove solids (glass, plastics etc.)
- Absorb powder with wet cloth/wipe and liquids with dry material
- Avoid formation of dust and aerosols
- Remove protective clothes from outside to inside
- Carefully wash hands

Spill management: Report

- Place, date, organization, department etc.
- Description of accident
- Type and amounts of released substance(s)
- Affected persons, type of personal contamination
- Contaminated areas, surfaces, objects
- Decontamination and cleaning measures
- Symptoms, report of doctor
- Results of ambient and biomonitoring

Spill management: Regular Training

Summary:

- **Release of substances not completely avoidable**
- **Contamination of the workplace frequently occurs**
- **Proper cleaning and spill management is important**
- **“Clean” working is possible even with high throughput**

- **<u>Monitoring can help to:</u>**
  - ***quantify contamination levels***
  - ***identify problematic spots, steps, practices etc.***
  - ***clarify mechanisms of release and spread***
  - ***control efficiency of counter measures***
  - ***lower contamination levels***

PharmaMonitor
Analysis-Cleaning-Training

www.Pharma-Monitor.de

Thank you for Your attention!

Questions ?