2012 Academy Seminar - Thessaloniki, Greece

DOs and DON´Ts in setting up a new facility

21 April 2012,

Barbara Wimmer,

barbara.wimmer@gespag.at

eahp
european association of hospital pharmacists
making the difference in medication use

Conflict of interest:

- nothing to disclose

eahp
european association of hospital pharmacists
making the difference in medication use

eahp
european association
of hospital pharmacists
making the difference in medication use

eahp
european association
of hospital pharmacists
making the difference in medication use

Design and completion in line with GMP

- Design qualification (DQ)
- Installation qualification (IQ)
- Operational qualification (OQ)
- Performance qualification (PQ)

Pharmacy entrance

Visitors have to register here

Pharmacy premises and equipment: DQ, IQ, OQ, PQ

Cleanroom garments

Underwear (long sleeves and long trousers)

Material: microfiber

Overall

Detachable hood

Over-boots

eahp
european association of hospital pharmacists
making the difference in medication use

REINHEITSKLASSEN

GMP / US-FED-STD 209 E (seit 2001 offiziell durch ISO ersetzt) / ISO 14644-1

comprei
CLEANROOM COMPETENCE CENTER

Klasse \ Größe			≥ 0,1 µm		≥ 0,2 µm		≥ 0,3 µm		≥ 0,5 µm		≥ 1 µm		≥ 5 µm	
GMP	US-FED-STD 209E	ISO	/ m³	/ ft³	/ m³	/ ft³	/ m³	/ ft³	/ m³	/ ft³	/ m³	/ ft³	/ m³	/ ft³
		Class 1	10		2		-	-	-	-	-	-	-	-
		Class 2	100	3	24	1	10		4		-	-	-	-
		Class 3	1.000	28	237	7	102	3	35	1	8		-	-
	1		1.240	35	265	7,5	106	3	35,3	1			-	-
		Class 4	10.000	283	2.370	67	1.020	29	352	10	83	2	-	-
	10		12.400	350	2.650	75	1.060	30	353	10			-	-
A									3.520	100			20	
B (r)									3.520	100			29	1
		Class 5	100.000	2.832	23.700	671	10.200	289	3.520	100	832	24	29	1
	100		-	-	26.500	750	10.600	300	3.530	100			-	-
		Class 6	1.000.000	28.317	237.000	6.711	102.000	2.888	35.200	997	8.320	236	293	8
	1000		-	-	-	-	-	-	35.300	1.000			247	7
B(o) / C(r)									352.000	9.968			2.900	82
		Class 7	-	-	-	-	-	-	352.000	9.968	83.200	2.356	2.930	83
	10.000		-	-	-	-	-	-	353.000	10.000			2.470	70
C(o) / D(r)									3.520.000	99.676			29.000	821
		Class 8	-	-	-	-	-	-	3.520.000	99.676	832.000	23.560	29.300	830
	100.000		-	-	-	-	-	-	3.530.000	100.000			24.700	700
		Class 9	-	-	-	-	-	-	35.200.000	996.758	8.320.000	235.597	293.000	8.297

Klasse	Partikel				Empfohlene Grenzwerte an "koloniebildenden Einheiten" (KBE) für die mikrobiologische Kontaminierung (a)			
	at rest		in operation		Luftprobe KBE/m³	Petrischalen (Ø 90 mm) KBE / 4 Stunden (b)	Kontaktplatten (Ø 55 mm) KBE / Platte	Handschuhabdruck 5 Finger KBE / Handschuh
	≥ 0,5 µm	≥ 5 µm	≥ 0,5 µm	≥ 5 µm				
A	3.520	20	3.520	20	< 1	< 1	< 1	< 1
B	3.520	29	352.000	2.900	10	5	5	5
C	352.000	2.900	3.520.000	29.000	100	50	25	-
D	3.520.000	29.000	nicht festgelegt	nicht festgelegt	200	100	50	-

a = hierbei handelt es sich um Durchschnittswerte
b = einzelne Petrischalen können auch weniger als 4 Stunden exponiert werden

Anmerkungen: (r): at rest; (o): in operation. Die m³- und ft³-Werte für den US-FED-STD wurden direkt aus dem US-FED-STD-209E übernommen. Die m³-Werte aus der ISO-Klassifizierung wurden mit dem Faktor 0,028317 multipliziert und auf ganze Zahlen gerundet und ergeben den Wert in ft³. **Alle Angaben ohne Gewähr.**

Cleanroom classes (figure source: comprei.com, March 2012)

	Maximum permitted number of particles per m^3 equal to or greater than the tabulated size			
	At rest		In operation	
Grade	**0.5 µm**	**5.0µm**	**0.5 µm**	**5.0µm**
A	3 520	20	3 520	20
B	3 520	29	352 000	2 900
C	352 000	2 900	3 520 000	29 000
D	3 520 000	29 000	Not defined	Not defined

	Recommended limits for microbial contamination (a)			
Grade	air sample cfu/m^3	settle plates (diameter 90 mm) cfu/4 hours (b)	contact plates (diameter 55 mm) cfu/plate	glove print 5 fingers cfu/glove
A	< 1	< 1	< 1	< 1
B	10	5	5	5
C	100	50	25	-
D	200	100	50	-

Notes
(a) These are average values.
(b) Individual settle plates may be exposed for less than 4 hours.

Cleanroom classes (figure source: EU Guidelines to Good Manufacturing Practice Medical Products for Human and Veterinary Use Annex 1)

Monitoring system in the clean rooms

On-line monitoring: Validated software

Particles (0,5µm and 5µm), down-flow, temperature, humidity, pressure differentials

eahp
european association of hospital pharmacists
making the difference in medication use

Clean room in Steyr

Material and waste pass-throughs

Laminar air flow safety work bench

eahp
european association of hospital pharmacists
making the difference in medication use

Cleanroom in Steyr

2nd workplace

eahp
european association of hospital pharmacists
making the difference in medication use

Commencing the project

Validation master plan (VMP)

- Type
- Scope and frequency

of validation activities

Risk assessment

Site master file (SMF)

- Detailed operational descriptions
- Organisational diagram

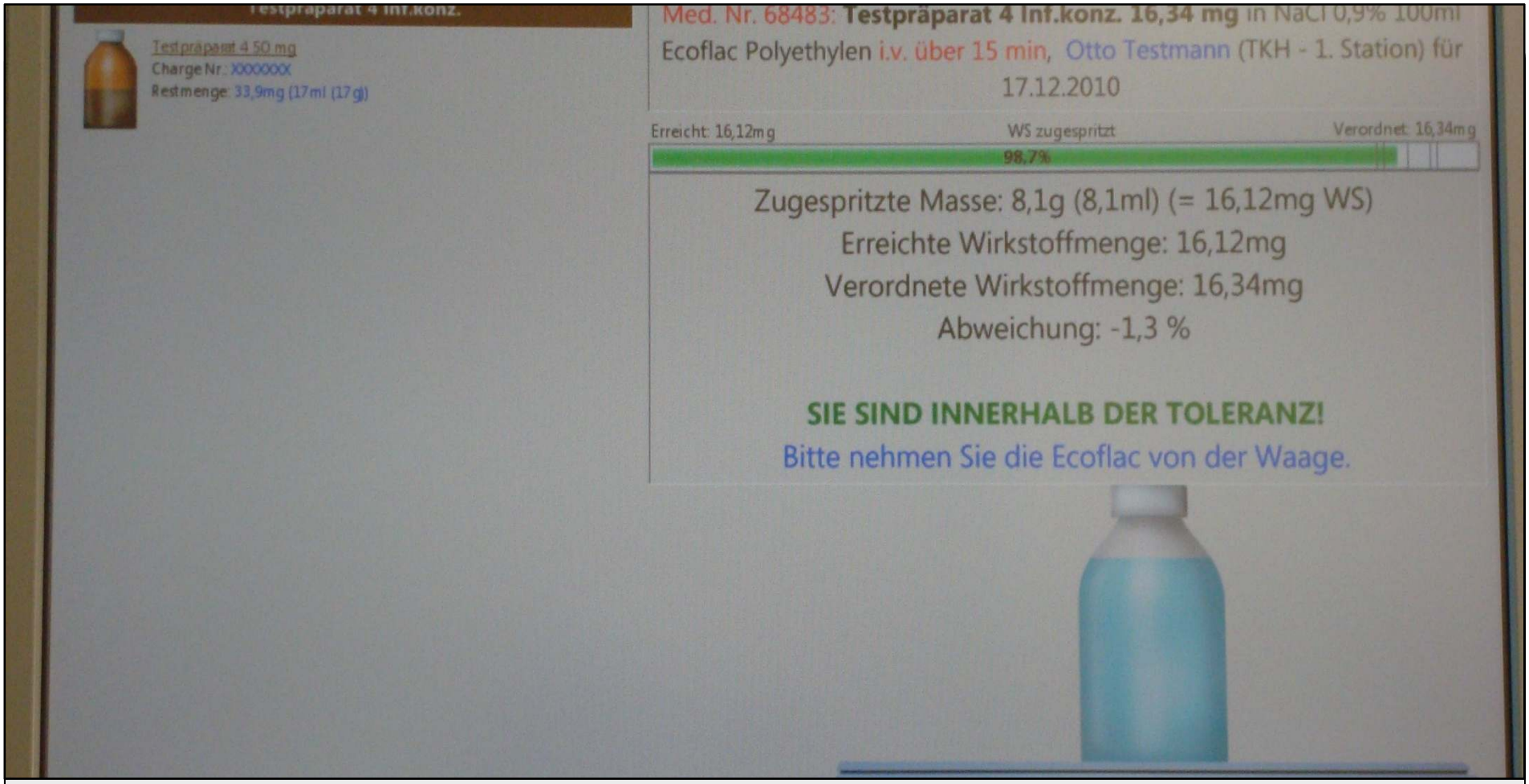
Work station descriptions

Standard operating procedures (SOPs)

Conducting process validation (media fills)

- Plan when to conduct the media fills, plan for new colleagues
- Annual revalidation

eahp
european association of hospital pharmacists
making the difference in medication use



Computer software CATO

For the compounding of cytotoxic drugs the software was also validated.

eahp
european association of hospital pharmacists
making the difference in medication use

Keeping certified status

- Maintenance
- Annual calibration
- Revalidation/requalification
- Guarantee of environmental standards
- Trend analysis

Training of employees/ new employees/technical staff/ cleaning staff

Documentation system

- Annual review of SOPs
- Change controls (CC)
- Risk assessment
- Deviation reports
- Audits

Miscellaneous

- Access and key concept: Make sure you define WHO gets WHAT access rights
- Plan enough room for storage
- A separate cleaning room can be very useful
- Make sure you have defined a way for your product approval
- Provide detailed plans for actions to be taken in event of a system failure
- Make sure you have appropriate IT/technical support

Working on the LAF

eahp
european association of hospital pharmacists
making the difference in medication use

Cytostatic drugs are sealed in foil

eahp
european association
of hospital pharmacists
making the difference in medication use

References

- Useful links:

http://www.gmp-compliance.org/eca_link_navigator.html

http://www.gmp-navigator.com/nav_guidelines.html

- DIN 12980 Laboreinrichtungen – Sicherheitswerkbänke für Zytostatika/Laboratory furniture – Safety cabinets for handling cytotoxic substances, 2005.
- EU Guidelines to Good Manufacturing Practice , Medical Products for Human and Veterinary Use, Volume 4, Annex 1 Manufacture of Sterile Medicinal Products, 2008.
- FDA Guidance for Industry Part 11, Electronic Records; Electronic Signatures – Scope and Application, 2003.
- Final Version of Annex 15 to the EU Guide to Good Manufacturing Practice, Qualification and Validation, 2001.
- ICH Q7 Good manufacturing practice guide for active pharmaceutical ingredients, 2000.
- ICH Q9 Quality risk management , 2005.
- PIC/S PE 009-9 Guide to good manufacturing practice for medicinal products, 2009.
- PIC/S PE 010-3 Guide to good practices for preparation of medicinal products in healthcare establishments, 2008.
- PIC/S PI 007-6 Recommendation on validation master plan installation and operational qualification non-sterile process validation cleaning validation, 2007.
- PIC/S PI 007-6 Recommendation on the validation of aseptic processes, 2011.
- PIC/S PI 011-3 Guidance Good practices for computerised systems in regulated “GXP” environments, 2007.
- Resolution CM/ResAP on quality and safety assurance requirements for medicinal products prepared in pharmacies for the special needs of patients, 2011.
- USP Pharmaceutical compounding – Sterile preparations, 2007.

Thank you very much for your attention!

Source photos: Pharmacy LKH Steyr

eahp
european association of hospital pharmacists
making the difference in medication use