Steinbeis Transferzentrum Tübingen
Arzneimittel – Kosmetika - Medizinprodukte

Certificate

We hereby certify, that the below mentioned production lines meet

all GMP-guidelines, EG –GMP-Annex 15 guideline
and PIC/S guideline PI 006-3 requirements.

Product lines: **D-, PUA, PTA45-, K-, M and**
PFA579, PFA579lift and
PFA779lift

Manufacturer: Mettler-Toledo (Albstadt) GmbH
Unter dem Malesfelsen 34
72458 Albstadt
Germany

Tübingen, May 21, 2010

Prof. Dr. Ingrid Müller

Elke Weber, M.Sc. Dipl. Ing. (FH)

Steinbeis Transferzentrum
Arzneimittel - Kosmetika - Medizinprodukte
Leiter: Prof. Dr. Ingrid Müller, Stellvertretender Leiter: Elke Weber (M.Sc, Dipl.Ing (FH))
Correnssstraße 34
72076 Tübingen
Tel.: 07071/37691
E-Mail: Ingrid.Mueller@stw.de, Elke.Weber@stw.de

1. Description of the product line

DN Line Bench scales

Bench scales with analog or digital interface. Load plate stainless steel.

Technology	DMS load cell (strain gauge, single point)
Weighing range [kg]	6, 15, 30, 60, 150, 300, 600
Platform sizes [mm]	240x300, 300x400, 400x500, 500x650, 600x800

DB-DCC

The DB-DCC-Line bench scales are built up hybrid – with a DMS-load cell and a lever arm system.

Technology	DMS load cell with lever arm system
Platform size [mm]	400x500, 600x800, 800x800, 1000x800
Weighing capacity [kg]	30, 60,150,300,600

DN- Line floor balances

Standard floor scales with screwed or foldable load plate.

Installation	Floor or pit mounted
Technology	Use of 4 DMS load cells
Platform size [mm]	1250x1000, 1500x1250, 1500x1500, optional: free sizes
Weighing capacity [kg]	300, 600, 1500, 3000

DRF/DSF

Flexible heavy goods scales, up to 3 modules.

Installation	Floor or pit mounted
	4 DMS load cells (1module)
Platform size [m]	1,5 - 2 x 1,5 - 6
Weighing capacity [kg]	3000, 6000, 12000 (only DSF)

Steinbeis Transferzentrum
Arzneimittel - Kosmetika - Medizinprodukte
Leiter: Prof. Dr. Ingrid Müller, Stellvertretender Leiter: Elke Weber (M.Sc, Dipl.Ing (FH))
Correnssstraße 34
72076 Tübingen
Tel.: 07071/37691
E-Mail: Ingrid.Mueller@stw.de, Elke.Weber@stw.de

PTA45-

Pallet scale for harsh environments.

Installation	Floor mounted
Technology	Use of 4 DMS load cells
Platform size [mm]	1260x600, optional: free sizes
Weighing capacity [kg]	300, 600, 1500, 3000

PTA459

PUA579

Low profile scale with minimum height of 35/45mm.

Installation	Floor mounted
Technology	4 DMS load cells
Material	Stainless steel AISI304- optional: AISI316
Platform size [mm]	850x850, 1500x1250, optional: free sizes
Weighing capacity [kg]	300, 600, 1500

PUA579

PFA579

The PFA579 floor scales are rugged and flexible.

Installation	Floor or pit mounted
Technology	4 DMS measuring cells
Material (load plate and frame)	Stainless steel AISI304- optional: AISI316
Weighing range [kg]	300-3000
Platform sizes [mm]	between 700x400 and 2000x1500

PFA579

Steinbeis Transferzentrum
Arzneimittel - Kosmetika - Medizinprodukte
Leiter: Prof. Dr. Ingrid Müller, Stellvertretender Leiter: Elke Weber (M.Sc, Dipl.Ing (FH))
Correnssstraße 34
72076 Tübingen
Tel.: 07071/37691
E-Mail: Ingrid.Mueller@stw.de, Elke.Weber@stw.de

PFA579lift

PFA579lift floor scales are provided with a foldable load plate. They are suitable for routine cleaning. The platforms can be individually configured and so adapted according the requirements of the clients.

Installation	Floor or pitmounted
Technology	4 DMS measuring cells
Material (Load plate and frame)	Stainless steel AISI304- optional: AISI316
Weighing range [kg]	300 – 3000
Platform sizes [mm]	between 800x800 and 1500x1500 mm
	Special sizes are available upon request

PFA579lift – with open load plate

PFA779lift

PFA779lift scales were developed in order to fulfill aspects of hygienic design. Therefore they can be used in hygienic sensitive areas.
The weighing bridges are cleanable inside and outside because of the foldable load plate. The weighbridges can be individually configured and therefore adapted according to the requirements of the clients.

Installation	Floor-mounted or pit-mounted
Technology	4 DMS measuring cells
Material (Load plate and frame)	Stainless steel AISI304- optional: AISI316
Weighing range [kg]	300 – 3000
Platform sizes [mm]	Between 800x800 and 1500x1500
	Special sizes are available upon request

PFA779lift - opened load plate

Steinbeis Transferzentrum
Arzneimittel - Kosmetika - Medizinprodukte
Leiter: Prof. Dr. Ingrid Müller, Stellvertretender Leiter: Elke Weber (M.Sc, Dipl.Ing (FH))
Correnssstraße 34
72076 Tübingen
Tel.: 07071/37691
E-Mail: Ingrid.Mueller@stw.de, Elke.Weber@stw.de

K-Line
The K-Line contains bench- and floor scales.


KES1500sk

Technology	Hybrid construction, electromagnetic force compensation measuring cell and lever arm system
Approved resolution	up to 15000e / 32000e
Platform size [mm]	
Bench Scales	280x350 to 600x800
Floor Scales	800x800 to 2000x1500
Weighing capacity [kg]	
Bench Scales	3 to 300
Floor Scales	300 to 6000

M-Line
The M-Line contains bench- and floor scales.


MCS600

Technology	Hybrid construction - digital DMS measuring cell and lever arm system.
Approved resolution	up to 3x3000e multi interval
Platform size [mm]	
Bench Scales	280x350 to 600x800
Floor Scales	800x800 to 1500x1500
Weighing capacity [kg]	
Bench Scales	15 to 300
Floor Scales	300 to 3000

Steinbeis Transferzentrum
Arzneimittel - Kosmetika - Medizinprodukte
Leiter: Prof. Dr. Ingrid Müller, Stellvertretender Leiter: Elke Weber (M.Sc, Dipl.Ing (FH))
Correnssstraße 34
72076 Tübingen
Tel.: 07071/37691
E-Mail: Ingrid.Mueller@stw.de, Elke.Weber@stw.de

2. General requirements for balances

Scales have to show the suitable measurement range and the required precision (EC-GMP guide[1], chapter 3.40).

They have to be calibrated regularly, which has to be documented (EC-GMP guide, chapter 3.41).

The permitted tolerance must be provided for the respective weighing capacity,

by consideration of the measuring inaccuracies, i.e. the still tolerated deviation of the debit value.

Working with raw materials, the equipment and the utensils used have to meet the requirements for surfaces in pharmaceutical production.

According to § 211.65 “Construction of the equipment”[2] of the FDA: *„(a) Equipment shall be constructed so that surfaces that contact components, in-process materials, or drug products shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements.”*

The cleaning ability is confirmed by the cleaning validation. Established cleaning instructions are necessary as a prerequisite for a cleaning validation.

The amount of permitted residuals whether active pharmaceutical ingredients or cleaning agents, is dependant on the preliminary manufactured product. These include the derivative product and the lot size of the derivative product. A first, general statement for not critical products can be made with the criteria "visual clean". According to the literature[3], backlogs of 375 µg per 100 cm² are no longer visible.

[1] EC-GMP guide, chapter 3.40

[2] USA 21 CFR Part 211

[3] Buscalferri et.al., Pharmind 62, Nr. 6 (2000)

Steinbeis Transferzentrum
Arzneimittel - Kosmetika - Medizinprodukte
Leiter: Prof. Dr. Ingrid Müller, Stellvertretender Leiter: Elke Weber (M.Sc, Dipl.Ing (FH))
Correnssstraße 34
72076 Tübingen
Tel.: 07071/37691
E-Mail: Ingrid.Mueller@stw.de, Elke.Weber@stw.de

3. Appraisal criteria for an optimal cleaning

General

In principle, those parts of equipment, which come into contact with the product, have to be cleaned well. Regarding the balances, these parts are the load plates.
Both the FDA inspection guideline for cleaning validation and the PIC guideline PIC/S 006-3 cite the visual criterion as one out of three possible acceptance criterions. From these the most appropriate criterion has to be chosen to appraise the cleaning success.
The balances of the product line D-, PUA, PTA45-, K-, M Line and PFA579, PFA579lift and PFA779lift were subjected to a qualified examination regarding "cleaning ability".[1] This means that the balances of the product lines D-, P- K-, M, PFA579, the PFA579lift and the PFA779lift must be free of visible residuals after cleaning. As a basis for this examination the works of Buscalferri, F., Assignation of the visibility limit of pharmaceutical active agents (“Bestimmung der Sichtbarkeitsgrenze von pharmazeutischen Wirkstoffen”), master thesis, Albstadt-Sigmaringen University, course of studies pharmaceutical technology (1999) and Fourman, G. L., Mullen, Determining Cleaning Validation Acceptance Limits for Pharmaceutical Manufacturing Operations , Pharm. Technol. 17 (4), 54 (1993) were used.

[1] The examinations and their evaluation were carried out by Prof. R. Ziegler.

Steinbeis Transferzentrum
Arzneimittel - Kosmetika - Medizinprodukte
Leiter: Prof. Dr. Ingrid Müller, Stellvertretender Leiter: Elke Weber (M.Sc, Dipl.Ing (FH))
Correnssstraße 34
72076 Tübingen
Tel.: 07071/37691
E-Mail: Ingrid.Mueller@stw.de, Elke.Weber@stw.de

Procedure

A granulated material, which was coloured with Erythrosine, was used as a sample. The examinations[1] were carried out according to the "visually clean" criteria (please see "GMP Berater" 8E (11)). First the load plates of the product lines D-, PUA, PTA45-, K-, M, PFA579, the PFA579lift and the PFA779lift were polluted, following by a cleaning step. A cleaning agent (P3-cosa PUR 80 Manufacturer: Ecolab GmbH & Co. OHG, Düsseldorf), which is commonly used in pharmaceutical production was taken and feigned according to different pollution degrees.
The cleaning success was then appraised visually.
In addition, a cast test was carried out before and after the cleaning to determine the complete microbial count.
The exact data can be taken from the SOP for cleaning and from the test report. These results show clearly, that the depletion degree meets in principle the hygienic requirements. In principle the depletion degree is dependent on the examined material and the specific requirements of the examination.

Results

In regard to the cleaning, the load plates of the product lines, D-, PUA, PTA45-, K-, M, the PFA579, the PFA579lift and the PFA779lift, correspond to the visually clean criteria. The cast test for the determination of the complete microbial count showed a significantly lower complete microbial count after the cleaning.

[1] These experiments were performed by Prof. Dr. R. Ziegler

Steinbeis Transferzentrum
Arzneimittel - Kosmetika - Medizinprodukte
Leiter: Prof. Dr. Ingrid Müller, Stellvertretender Leiter: Elke Weber (M.Sc, Dipl.Ing (FH))
Correnssstraße 34
72076 Tübingen
Tel.: 07071/37691
E-Mail: Ingrid.Mueller@stw.de, Elke.Weber@stw.de

Summary

The balances and terminals of the product lines, D-, PUA, PTA45-, K-, M, PFA579, the PFA579lift and the PFA779lift are GMP-compliant. The cleaning of the parts, which come in contact with the product (load plate), has to be carried out well. There aren't any heavily accessible places in which dust could accumulate. The load plate is removable, so that the cleaning of the parts which are not in contact with the product is guaranteed.
The PFA579lift and the PFA779lift are easy to clean as well. Every part is easily accessible. The mechanic components are constructed according to the GMP guidelines.

Steinbeis Transferzentrum
Arzneimittel - Kosmetika - Medizinprodukte
Leiter: Prof. Dr. Ingrid Müller, Stellvertretender Leiter: Elke Weber (M.Sc, Dipl.Ing (FH))
Correnssstraße 34
72076 Tübingen
Tel.: 07071/37691
E-Mail: Ingrid.Mueller@stw.de, Elke.Weber@stw.de

4. Appraisal factors for qualification

General

The PIC/S guideline PI 006-3 and the EG-GMP guide Annex 15 mention principles for qualification and validation.
Every machine or equipment which directly or indirectly influences the quality of the product shall be qualified. The machine or equipment shall be designed in agreement with the prevailing GMP guidelines. The machine shall be installed in agreement with the design specification and the functions shall be checked with the available documentation (functional qualification).

Procedure

The available documentation of the Mettler Toledo product lines, D-, PUA, PTA45-, K-, M, PFA579, the PFA579lift and the PFA779lift was checked to the effect of whether design qualification, installation qualification and functional qualification are feasible.

Steinbeis Transferzentrum
Arzneimittel - Kosmetika - Medizinprodukte
Leiter: Prof. Dr. Ingrid Müller, Stellvertretender Leiter: Elke Weber (M.Sc, Dipl.Ing (FH))
Correnssstraße 34
72076 Tübingen
Tel.: 07071/37691
E-Mail: Ingrid.Mueller@stw.de, Elke.Weber@stw.de

Results

The documentation of the Mettler Toledo product lines, D-, PUA, PTA45-, K-, M, PFA579, the PFA579lift and the PFA779lift is very detailed. Also an exact description of the balances with design drawings is available. The materials used are described precisely.
GMP-relevant documents are available (e.g. inspection certificate, CE-mark). Particulars regarding the maintenance are furnished.

Summary

The documentation of the manufacturer of the Mettler Toledo product lines, D-, PUA, PTA45-, K-, M, PFA579, the PFA579lift and the PFA779lift is written in a very detailed way and offers the necessary conditions for the execution of qualification, as it is demanded by EG-GMP guide Annex 15 and PIC/S guideline PI 006-3.

Steinbeis Transferzentrum
Arzneimittel - Kosmetika - Medizinprodukte
Leiter: Prof. Dr. Ingrid Müller, Stellvertretender Leiter: Elke Weber (M.Sc, Dipl.Ing (FH))
Correnssstraße 34
72076 Tübingen
Tel.: 07071/37691
E-Mail: Ingrid.Mueller@stw.de, Elke.Weber@stw.de