Fraunhofer Institute for Manufacturing
Engineering and Automation IPA

Director
Prof. Dr.-Ing. Thomas Bauernhansl

Nobelstraße 12
70569 Stuttgart

Phone +49 711 970-00
Fax +49 711 970-1399

Test report

Cleanliness suitability and cleanroom suitability tests at Fraunhofer IPA

Customer: Brecon Cleanroom Systems B.V.
Droogdokkeneiland 7
5026 SP Tilburg
The Netherlands

Project Manager: Dr.-Ing. Frank Bürger

Project Assistants: Dipl.-Ing. (FH) Sebastian Eiband
CTA Andrew Schönhaar
M.Sc. Vanessa Pfenning
Dipl.-Ing. (FH) Marion Schweizer
CTA Lisa Wiesner
LTA Gabriela Baum

Report No. **BR 1804-1024**

Stuttgart, Germany, Juli 23, 2018

Fraunhofer IPA

Index

1	**Introduction and objectives**	**5**
2	**Overview of the measurements**	**6**
3	**Overview of results**	**9**
4	**Airborne particle emission tests**	**11**
4.1	General information	11
4.2	Cleanroom environment	12
4.3	Test set-up and parameters	12
4.3.1	Test set-up and parameters to simulate typical stress on the test piece	14
4.3.2	Structure-borne sound applied to the upperside of TP01	16
4.4	Measuring equipment	19
4.5	Localization tests	19
4.6	Qualification measurements	20
4.6.1	Procedure	20
4.6.2	TP01 inside: description of the measuring points MP01 to MP19	21
4.6.3	TP01 outside: description of the measuring points MP20 to MP34	23
4.6.4	Analysis of the results from the airborne particle emission tests	24
4.6.5	Course of particle emissions over time	24
4.7	Classification	30
4.7.1	Statistical verification of the test results	30
4.7.2	Mean and maximum particle emission values and classification	31
4.8	Summary of the classification results	40
4.9	Annex: comparison of different classifications of airborne particulate contamination	42
5	**Determination of resistance to chemicals**	**43**
5.1	Test conditions	43
5.2	Analyzed sample	43
5.3	Test procedure	44
5.4	Assessment criteria	46
5.4.1	Assessment of the amount of damage	46
5.4.2	Assessment of the size of damage	47
5.4.3	Assessment of the intensity of alteration	47
5.4.4	Reagents utilized	48
5.4.5	Microscopic assessment	48

5.4.6 Classification according to VDI 2083 Part 17 48
5.5 Results of the chemical resistance tests TP02 49
5.5.1 Formalin 37 % 50
5.5.2 Ammoniac 25 % 51
5.5.3 Hydrogen peroxide 30 % 52
5.5.4 Sulfuric acid 5 % 53
5.5.5 Phosphoric acid 30 % 54
5.5.6 Peracetic acid 15 % 55
5.5.7 Hydrochloric acid 5 % 56
5.5.8 Isopropanol 100 % 57
5.5.9 Sodium hydroxide 5 % 58
5.5.10 Sodium hypochlorite 5 % 59
5.6 Results of the chemical resistance tests TP03 60
5.6.1 Formalin 37 % 61
5.6.2 Ammoniac 25 % 62
5.6.3 Hydrogen peroxide 30 % 63
5.6.4 Sulfuric acid 5 % 64
5.6.5 Phosphoric acid 30 % 65
5.6.6 Peracetic acid 15 % 66
5.6.7 Hydrochloric acid 5 % 67
5.6.8 Isopropanol 100 % 68
5.6.9 Sodium hydroxide 5 % 69
5.6.10 Sodium hypochlorite 5 % 70
5.7 Summary of results of the chemical resistance tests 71
6 H_2O_2 absorption and desorption behavior 73
6.1 Experimental design 73
6.2 Measurement strategy 74
6.2.1 K-value 74
6.3 Results 75
6.3.1 Blank value 75
6.3.2 Granite Standard Coil Coated Steel 76
6.3.3 Formica High Pressure Laminate 77
6.4 k-values 77

Fraunhofer IPA

7 Assessment of conformity with GMP regulations and EHEDG conception and design recommendations 78

7.1 Requirements 78
7.1.1 Generation and cause of contamination 79
7.1.2 Removing contamination 80
7.1.3 Materials and surfaces 80
7.1.4 Design and geometry 81
7.2 Assessment of the test piece 82
7.3 Materials implemented 83
7.4 Assessment of details TP01 84
7.4.1 Wall and ceiling panels 84
7.4.2 Material joints 85
7.4.3 Connecting profiles 86
7.4.4 Floor connection profile 87
7.4.5 Transition between corner profile and floor connection profile 88
7.4.6 Transition between glass elements and wall / door 89
7.4.7 Air duct 90
7.4.8 Door 91
7.4.9 Door handle 92
7.4.10 Door hinges 93
7.4.11 Door seal 94
7.4.12 Interlock control panel 95
7.5 GMP and hygiene assessment 96
7.5.1 General information 96
7.5.2 GMP cleanliness classes 96
7.5.3 Suitability of operating utilities for use in the various GMP cleanliness classes 99
7.6 Summary 100

1 Introduction and objectives

Brecon Cleanroom Systems B.V. offers dust-free, germ-proof cleanroom systems. The products are manufactured under high quality standards and successfully implemented in a wide range of industries.

To secure the market position of Brecon Cleanroom Systems B.V. in the sector of clean manufacturing areas, it is essential to understand the contamination behavior of their products. Therefore, a wall / ceiling system need to be examined and assessed for cleanliness- and cleanroom suitability.

2 Overview of the measurements

The following tables show the exact breakdown of the test pieces:

TP01	
Description of test piece	Brecon Cassette Panel System
Description of test piece (short form)	BCPS
Composed of:	
Article number / Description	BM-W-SHC-101 / Wall Panel Steel Standard Coated HC BM-W-SRW-102 / Wall Panel Steel Standard Coated RW BM-W-HRW-101 / Wall Panel HPL Standard RW BM-W-H-air-101 / Wall Panel HPL Airduct 500m3 BM-D-131 / Steel Door with Window and Dropseal BM-D-117 + BM-D-118 / Built-in Doorcloser BM-K-101 / Aluminum Doorframe BM-G-101 / Window Standard 120x100x70 Safety glass BM-P-104 / Ceiling Panel Steel Standard Coated RW BM-W-SH-108 / PRO 3 Sealant BM-W-SH-106 / Aluminum Corner Profile BM-W-SH-102 / Aluminum Floor Profile BM-W-SH-109 / Round Corner Profile 65mm (massiv) BM-D-139 / Inter Lock Control Panel
Company name	Brecon Group
Color Panels:	RAL 9010
Category **Subcategory**	Cleanroom Facilities Wall / Ceiling / Floor / Door
Manufacturing date	4/2018

Figure 1 Test piece data TP01

TP02	
Description of test piece	Granite Standard Coil Coated Steel
Description of test piece (short form)	Coil Coated Steel
Company name	Brecon Group
Category Subcategory	Materials Metals
Article number	BM-W-SHC-101
Batch number	21705697 02
Manufacturing date	4/2018

Figure 2 Test piece data TP02

TP03	
Description of test piece	Formica High Pressure Laminate
Description of test piece (short form)	HPL
Company name	Brecon Group
Category Subcategory	Materials Material Composites
Article number	BM-W-HRW-101
Batch number	1285727
Manufacturing date	4/2018

Figure 3 Test piece data TP03

Fraunhofer IPA

The following table shows the corresponding tests carried out on all test pieces:

	Particle emission	ESD behavior	Outgassing	Chemical resistance	Cleanability (particles)	H_2O_2 absorption/desorption	Biological resistance	Surface roughness	Expertise
TP01	X								X
TP02				X		X			
TP03				X		X			

Figure 4 Table of test pieces and corresponding tests

3 Overview of results

TP01: **Particle emission** (ISO 14644-1, -14)	
Test parameter(s)	**Air Cleanliness Class**
Structure-borne noise = approx. 5 to 50 Hz	3
Overall result	**3**

TP01: **GMP** (EU GMP Annex 1; EHEDG Doc. 8; DIN EN 1672-2; ISO 14159)
Suitability
up to GMP Class A

TP02: **Chemical resistance** (ISO 2812-1;4628-1)				
Chemical resistance	1 h	3 h	6 h	**24 h**
Formalin 37%	0	0	0	**0**
Ammoniac 25%	0	0	0	**0**
Hydrogen peroxide 30%	0	0	0	**0**
Sulfuric acid 5%	0	0	0	**0**
Phosphoric acid 30%	0	0	1	**1**
Peracetic acid 15%	0	0	1	**1**
Hydrochloric acid 5%	0	0	0	**0**
Isopropanol 100%	0	0	0	**0**
Sodium hydroxide 5%	0	0	0	**0**
Sodium hypochlorite 5%	0	0	0	**0**

TP02: **Hydrogen peroxide absorption/desorption** (VDI 2083 Blatt 20)		
Ø k-value [min]	**Standard deviation** [min]	**Classification**
5.1	0.5	**fast**

Fraunhofer IPA

TP03: Chemical resistance (ISO 2812-1; 4628-1)				
Chemical resistance	1 h	3 h	6 h	**24 h**
Formalin 37%	0	0	0	**0**
Ammoniac 25%	0	0	0	**0**
Hydrogen peroxide 30%	0	0	0	**0**
Sulfuric acid 5%	0	0	0	**0**
Phosphoric acid 30%	0	0	0	**0**
Peracetic acid 15%	1	4	5	**5**
Hydrochloric acid 5%	0	0	0	**0**
Isopropanol 100%	1	1	1	**1**
Sodium hydroxide 5%	0	0	0	**0**
Sodium hypochlorite 5%	0	0	0	**0**

TP03: Hydrogen peroxide absorption/desorption (VDI 2083 Blatt 20)		
Ø k-value [min]	**Standard deviation** [min]	**Classification**
11.5	0.9	**fast**

Figure 5 Overview of results

4 Airborne particle emission tests

4.1 General information

A major criterion in clean and hygienic areas in industry and research is the concentration of airborne particles. Besides the quantity of particles per unit of volume of air, the size distribution of the particles is also critical when it comes to fulfilling cleanliness requirements.

Cleanliness requirements are set against the release of particles from the operating utilities used in clean or hygienic areas. The cause of particle emissions from operating utilities is generally tribological stress, which leads to wear and the generation and release of particles.

To determine the release of particles from operating utilities, particle emission measurements can be conducted in a test cleanroom with a low-turbulence displacement airflow following the procedure laid down in ISO 14644-14. The results enable the suitability of operating utilities to be determined for use in discrete air cleanliness classes according to ISO 14644-1. The VDI 2083 series uses the term **cleanroom suitability** to describe the suitability of operating utilities for discrete air cleanliness classes. Cleanroom suitability is one aspect of **cleanliness suitability**, which also includes all other cleanliness criteria relevant to a process. Apart from the release of particles, other cleanliness suitability criteria are, for example, chemical resistance, biological resistance, microbicidity and outgassing from materials, as well as the cleanability and hygienic design of components or equipment.

In the case of operating utilities such as manufacturing equipment, particle emission measurements serve not only to determine the influence of these systems on the environment (protection of the cleanroom) but also on the interior of the equipment itself (protection of the product).

By conducting localized particle emission measurements with optical particle counters in a test cleanroom with a low-turbulence displacement airflow, the cause of high particle emissions can be derived from the results obtained from the various measuring points.

4.2 Cleanroom environment

All tests are carried out in the Fraunhofer IPA competence center for ultraclean technology and micromanufacturing. Measurements are performed in a cleanroom fulfilling Class 1 specifications (in accordance with ISO 14644-1).
A vertical low-turbulence displacement airflow prevails in the cleanroom. Air is introduced via the ceiling and extracted via a raised floor. The velocity of the flow of first air (filtered air introduced into the cleanroom) is 0.45 m/s. Environmental conditions in the cleanroom are kept constant with a room temperature of 22 °C ± 0.5 °C and a relative humidity of 45 % ± 5 %.

According to ISO 14644-1, Cleanroom Class 1 means that only ten particles the size of 0.1 µm may be found a reference volume of one cubic meter. In practical operation, even fewer particles are found in this cleanroom class.

4.3 Test set-up and parameters

Test set-up
The customer supplied Fraunhofer IPA with the test piece. The test piece was suitable for continuous, maintenance-free operation.

On delivery, the test piece was introduced into the cleanroom at the Fraunhofer IPA in Stuttgart. It was then assembled and put into operation (complete with all the functional components required for its assembly and operation) by the customer.

Transfer of the test piece into the cleanroom
The test piece was brought into the cleanroom. In doing so, all surfaces and other functional elements were first wiped clean with low particle emission cleanroom cloths soaked in a mixture of isopropanol and DI-water and then dried with a jet of ionizing purified compressed air.

Pre-conditioning the test piece
The test piece was first operated in the reference cleanroom with a typical average load for a period of 24 hours while exposed to a flow of clean first air. In this way, the raised quantity of particles emitted during the running-in phase, which is not representative as far as later operation is concerned, is not included in the assessment.

Test parameters
To determine particle emissions from the test piece, it was operated using the parameters specified below.

The operating parameters selected for the test piece were arranged with the customer before the start of the project:

- structure-borne noise: .... approx. 5 to 50 Hz
- Ceiling
  - Oscillation velocity (Ø): .... v_1 = 992.4 µm/s
  - Oscillation acceleration (Ø): .... a_1 = 243 mm/s²
  - Oscillation of the system (Ø): .... s_1 = 169 µm
- Door End
  - Oscillation velocity (Ø): .... v_2 = 5762.0 µm/s
  - Oscillation acceleration (Ø): .... a_2 = 85 mm/s²
  - Oscillation of the system (Ø): .... s_2 = 1277 µm
- Wall HPL
  - Oscillation velocity (Ø): .... v_3 = 2248.0 µm/s
  - Oscillation acceleration (Ø): .... a_3 = 233 mm/s²
  - Oscillation of the system (Ø): .... s_3 = 538 µm
- Wall powder-coated steel panel
  - Oscillation velocity (Ø): .... v_4 = 2278.3 µm/s
  - Oscillation acceleration (Ø): .... a_4 = 65 mm/s²
  - Oscillation of the system (Ø): .... s_4 = 567 µm

Overview of the test set-up and test piece

Figure 6 Overview of the test set-up and test piece TP01

4.3.1 Test set-up and parameters to simulate typical stress on the test piece

For the airborne particle emission tests, the test piece is assembled onto an aluminum profile forming part of a specially-designed test set-up.

In cleanrooms, constructional elements are generally subjected to oscillations and structure-borne noise from the air-filtering system. These usually lie between approx. 5 Hz and 50 Hz. In order to achieve stress conditions similar to those encountered in reality, an oscillation generator capable of subjecting the ceiling systems to a modulating sinus oscillation with a frequency of f=50 Hz was utilized. The amplitude of the modulation was set to induce an oscillation velocity of approx. 1.0 * 10mm/s (effective value) on the upper surface of the systems (building surface of the test pieces).

The corresponding effective values of oscillation acceleration a (in m/s²) are shown in the following Figure. They are measured on the upper surface of the system. Compared with the typical value of approx. 0.005 mm/s which is applied in reality, the oscillation velocity was increased in order to obtain a higher level of certainty of the test results. The structureborne noise applied is thus to be viewed as being a „worst-case“ scenario.

The following figures show the test set up with the oscillation generator and a gauge for measuring structure-borne noise:

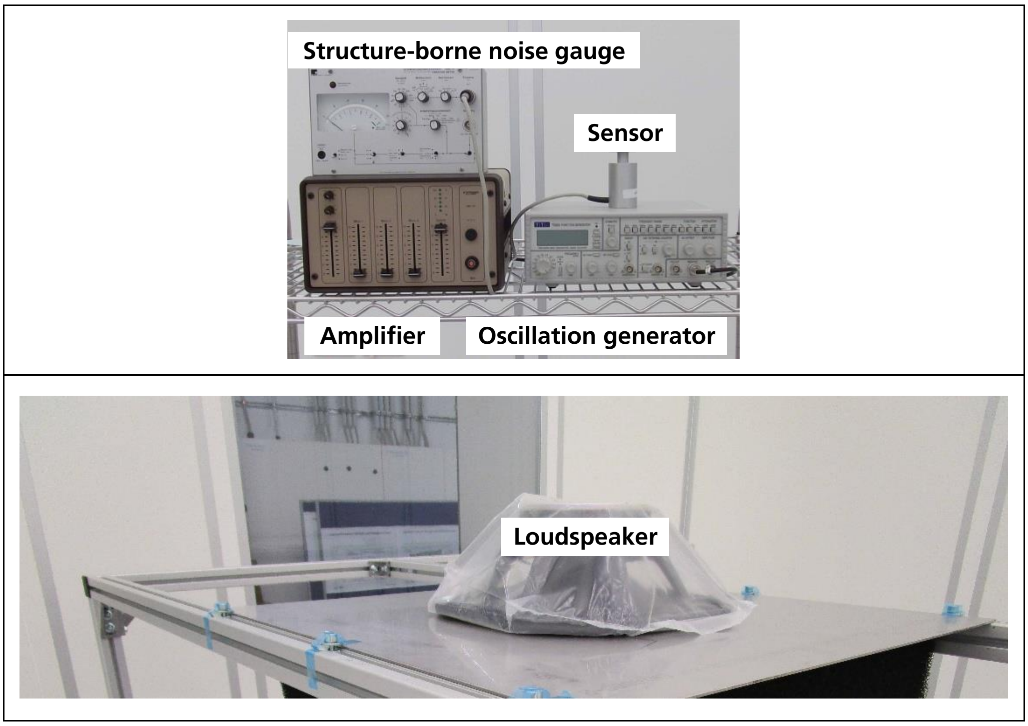


Figure 7 Test set-up with oscillation generator and gauge for measuring structure-borne noise

4.3.2 Structure-borne sound applied to the upperside of TP01

The following diagram illustrates the points where oscillation measurements were taken on the upperside of TP01:

4.3.2.1 Ceiling

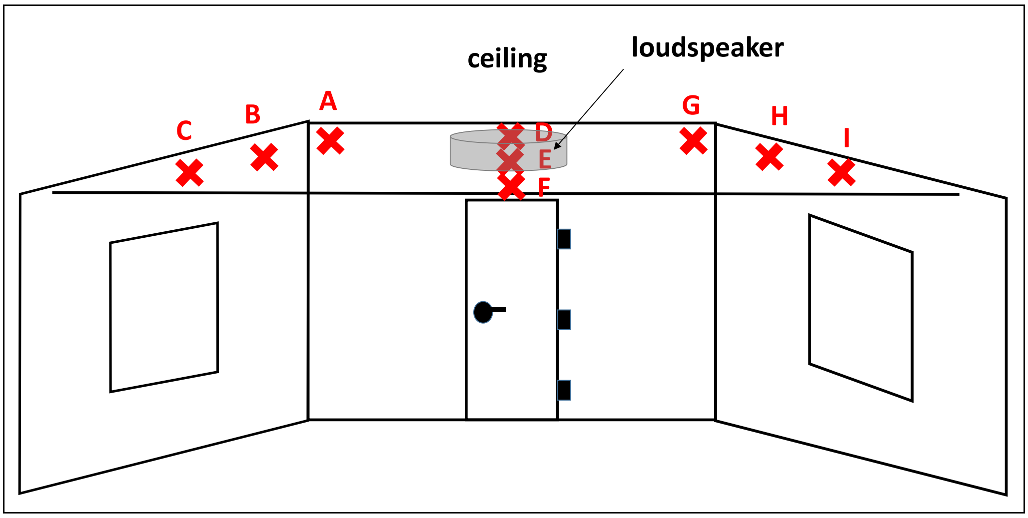


Figure 8 Measuring points where structure-borne sound was measured on the upperside of TP01

The figure below shows the mean values of the parameters measured when structure-borne sound was applied to the upperside of TP01:

ceiling			
TP01 MP	Oscillation velocity v [µm/s]	Oscillation acceleration a [mm/s²]	Oscillation of the system s [µm]
MPA	851,0	102	891
MPB	1270,0	62	138
MPC	200,0	73	17
MPD	1240,0	295	151
MPE	2160,0	638	116
MPF	2020,0	562	164
MPG	207,0	116	15
MPH	331,0	126	12
MPI	653,0	211	13
Average	**992,4**	**243**	**169**

Figure 9 Oscillation velocity and acceleration as well as oscillation of the system on the upperside of TP01

4.3.2.2 Door end

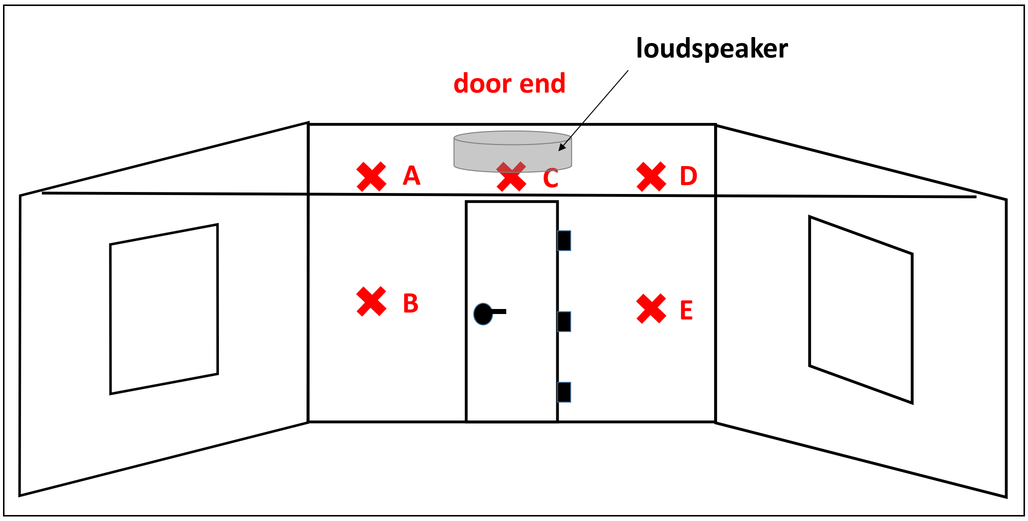


Figure 10 Measuring points where structure-borne sound was measured on the upperside of TP01

The figure below shows the mean values of the parameters measured when structure-borne sound was applied to the upperside of TP01:

door end			
TP01 MP	Oscillation velocity v [µm/s]	Oscillation acceleration a [mm/s²]	Oscillation of the system s [µm]
MPA	437,0	85	216
MPB	153,0	96	12
MPC	2290,0	82	638
MPD	9330,0	73	2600
MPE	16600,0	87	2920
Average	**5762,0**	**85**	**1277**

Figure 11 Oscillation velocity and acceleration as well as oscillation of the system on the upperside of TP01

4.3.2.3 Wall

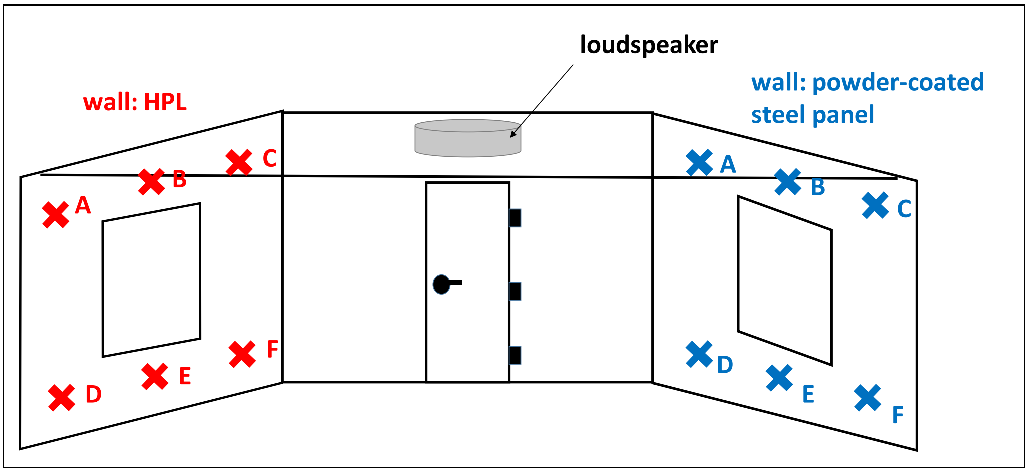


Figure 12 Measuring points where structure-borne sound was measured on the upperside of TP01

The figure below shows the mean values of the parameters measured when structure-borne sound was applied to the upperside of TP01:

wall: HPL			
TP01 / MP	Oscillation velocity v [µm/s]	Oscillation acceleration a [mm/s²]	Oscillation of the system s [µm]
MPA	513,0	130	200
MPB	661,0	72	115
MPC	5690,0	97	1200
MPD	794,0	105	407
MPE	700,0	91	363
MPF	5130,0	902	944
Average	**2248,0**	**233**	**538**

Figure 13 Oscillation velocity and acceleration as well as oscillation of the system on the upperside of TP01

wall: powder-coated steel panel			
TP01 / MP	Oscillation velocity v [µm/s]	Oscillation acceleration a [mm/s²]	Oscillation of the system s [µm]
MPA	1660,0	34	1110
MPB	3800,0	111	473
MPC	3350,0	172	495
MPD	1600,0	25	495
MPE	1460,0	24	380
MPF	1800,0	25	447
Average	**2278,3**	**65**	**567**

Figure 14 Oscillation velocity and acceleration as well as oscillation of the system on the upperside of TP01

4.4 Measuring equipment

In the tests to determine particle emissions, the following type of laser particle measuring device was used.

Type LasAir II 110 / LasAir III 110 from PMS with the measuring ranges of ≥ 0.1 µm, ≥ 0.2 µm, ≥ 0.3 µm, ≥ 0.5 µm, ≥ 1.0 µm and ≥ 5.0 µm.

Note: Due to the available particle size channels of ≥ 0.3 µm, particle emission tests according to ISO 14644-14 only give statistically assured information about the air cleanliness classes achieved ≥ ISO-Klasse 3 according to ISO 14644-1.

Optical particle counters function according to the principle of scattered light. Via a sampling probe, a defined volume of air of 1 cubic foot (1 cft = 28.3 liters) is sucked in every minute and guided into a measuring chamber via a tube connected to it. The air sucked in is illuminated by a light source - in modern devices either a laser or laser diode. As soon as a particle carried by the airflow is struck by the beam of light, light is scattered and recorded by photo-detectors.

The number of impulses recorded corresponds with the number of particles present in the volume of air. The amplitude of the impulses indicates the particle size.

4.5 Localization tests

To select the measuring points for the subsequent qualification tests, separate localization tests were performed for each set of parameters.

Critical contamination sites (these are generally areas subjected to tribological stress, such as bearings slits) were systematically investigated for particle emissions, taking into consideration the motion sequences planned. The surface of the test piece was also visually assessed. By comparing the values obtained, sites could be identified where especially high levels of particulate emission were generated during motion sequences. A particle measuring probe was carefully positioned at these sites to detect the maximum number of particles being emitted from the test object.

4.6 Qualification measurements

4.6.1 Procedure

The qualification tests were performed according to ISO 14644-14.

Measuring probes were placed at each of the critical sites identified (= measuring points). At each measuring point, particle emission measurements were recorded with measuring intervals of 1/min over a period of 100 minutes. To better compare results, up to 19 particle counters were used in parallel at up to 19 different measuring points for each test series to record particle emission values.

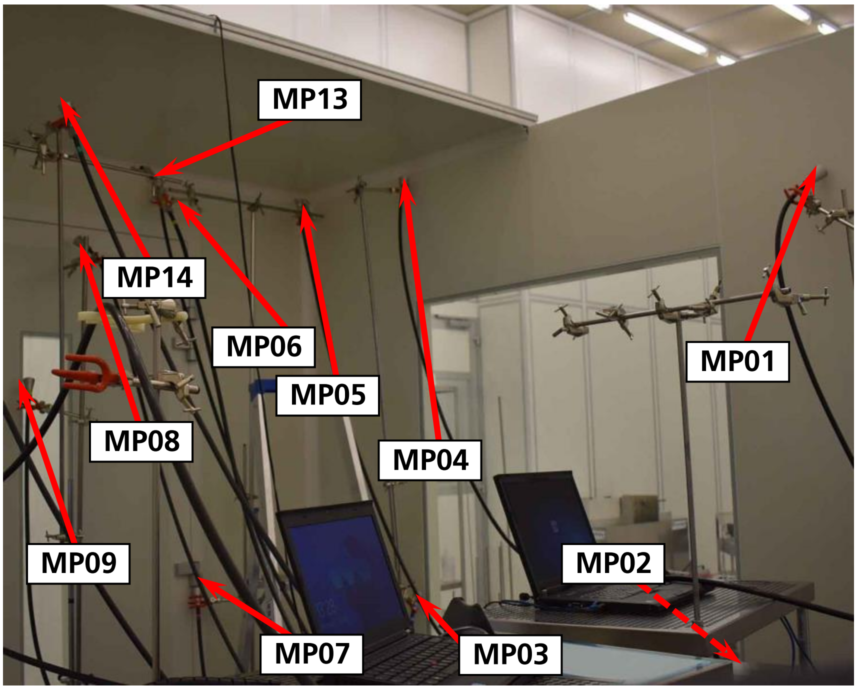
The measurement volume is sucked in at a rate of 1 cft/min. Particle measurements are shown cumulatively for each particle size channel, i.e. the figure shown for a particle size channel refers to all particles equal to or larger than the particle size channel stated (≥ 0.1 µm, ≥ 0.2 µm, ≥ 0.3 µm, ≥ 0.5 µm, ≥ 1.0 µm or ≥ 5.0 µm).

The selected time of 100 minutes ensures adequate statistical certainty of the test results and safeguards against faulty measurements. Each measurement value contains information about the particle size, the quantity of particles generated and the site where the particles were emitted.

The results were analyzed statistically conform to the procedure described in the guideline ISO 14644-14, thus enabling the suitability of the operating utility for use in cleanrooms classified according to ISO 14644-1 to be determined.

4.6.2 TP01 inside: description of the measuring points MP01 to MP19

The following photographs show the exact points selected to measure airborne particles emitted from the test piece.



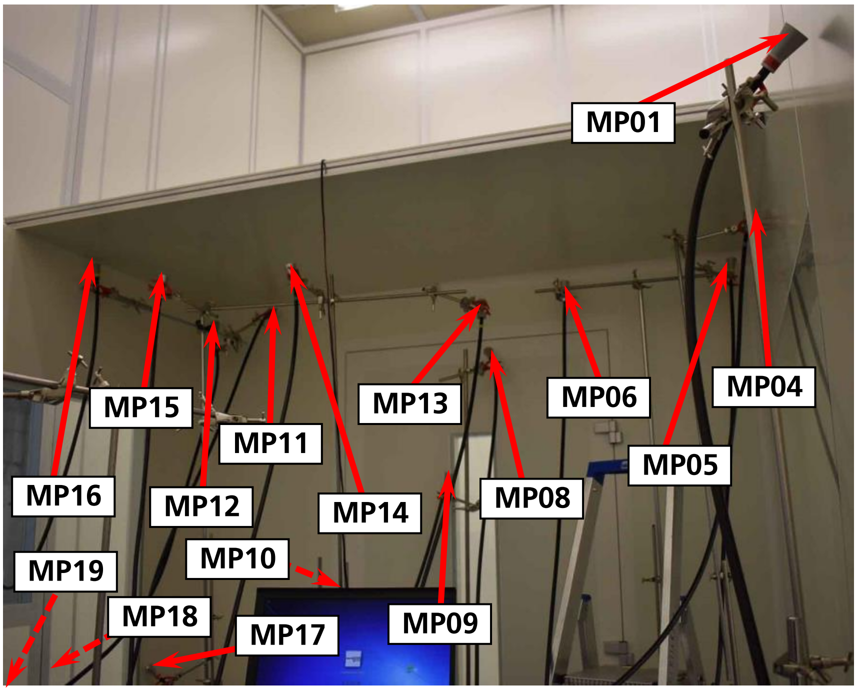


Figure 15 Measuring points MP01 to MP19 selected to measure airborne particle emissions from TP01

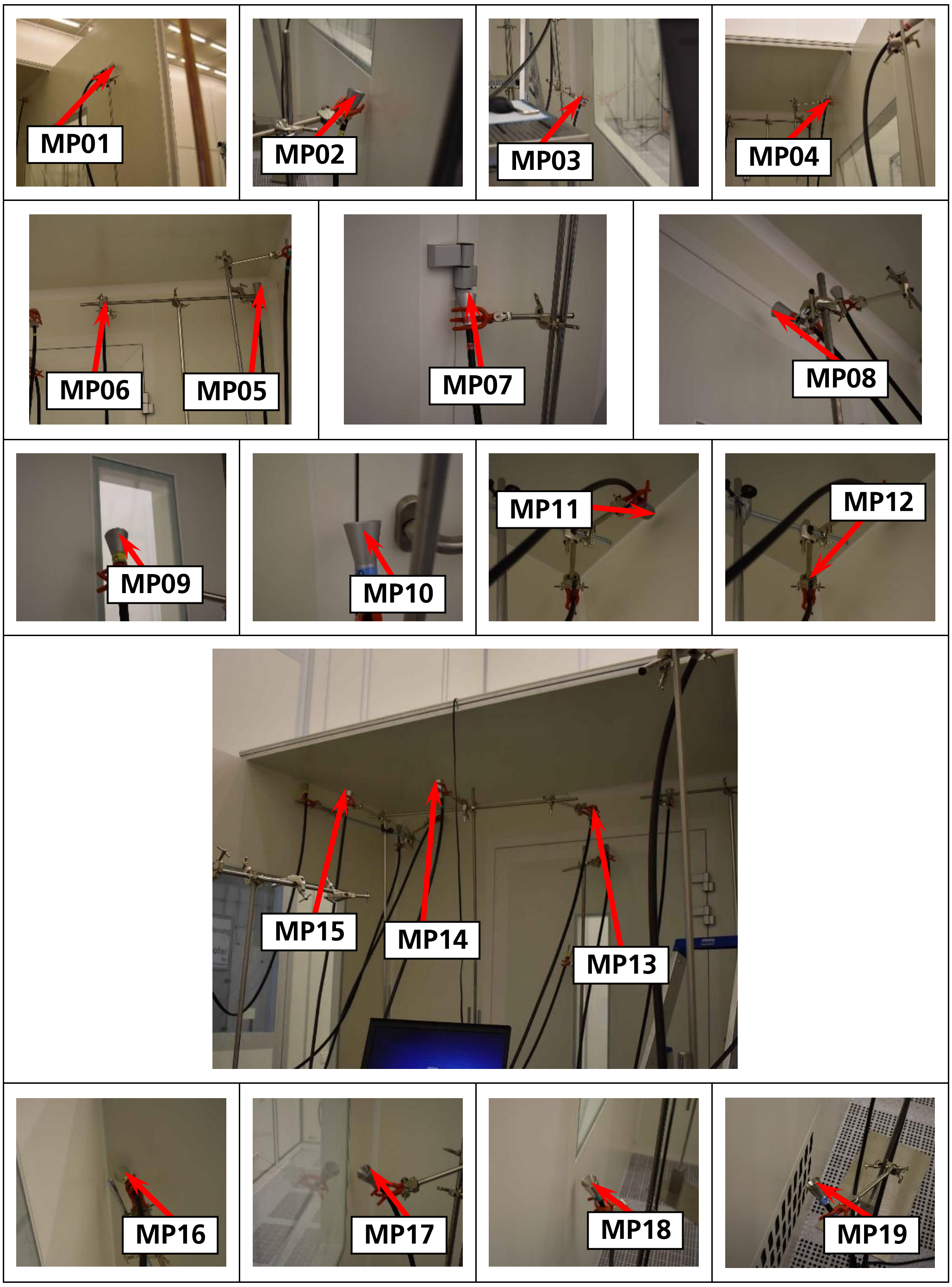


Figure 16 Measuring points MP01 to MP19 selected to measure airborne particle emissions from TP01

4.6.3 TP01 outside: description of the measuring points MP20 to MP34

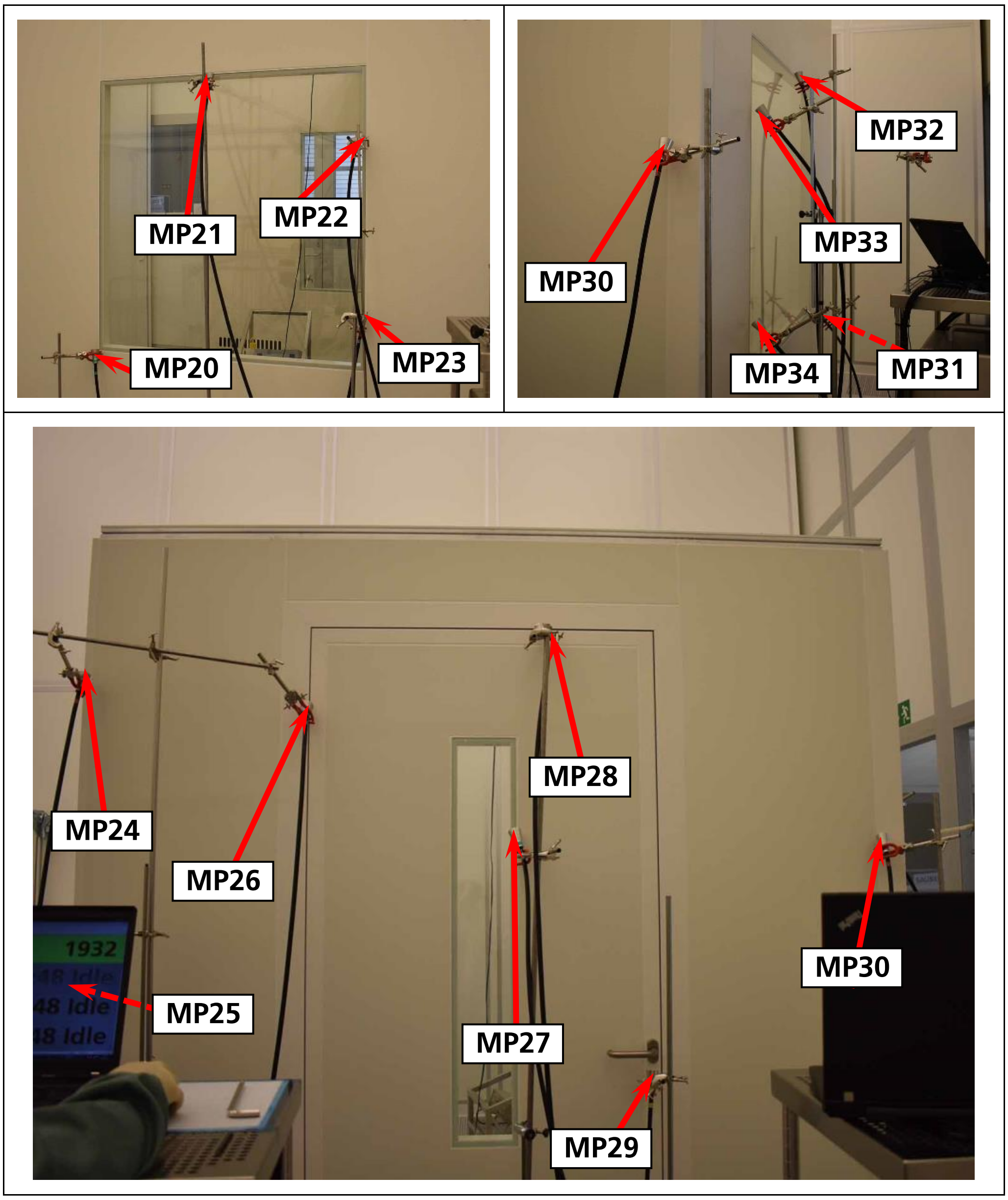


Figure 17 Measuring points MP20 to MP34 selected to measure airborne particle emissions from TP02

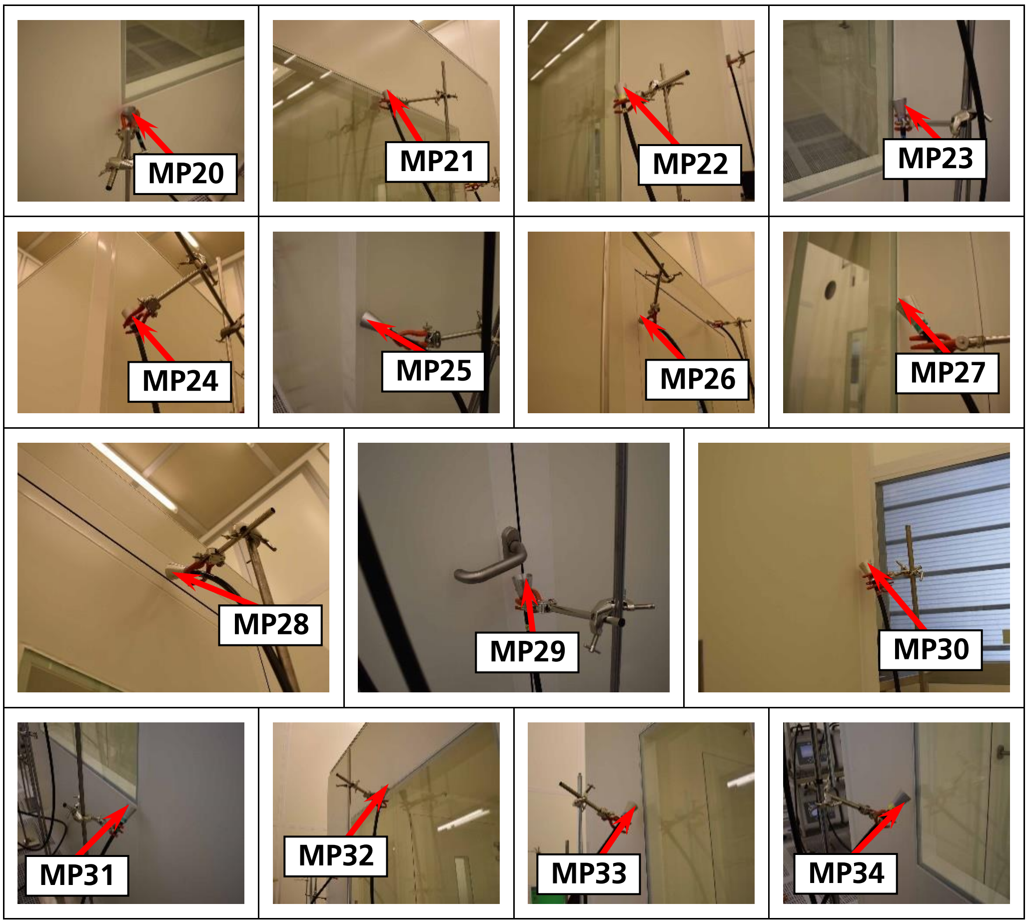


Figure 18 Measuring points MP20 to MP34 selected to measure airborne particle emissions from TP02

4.6.4 Analysis of the results from the airborne particle emission tests

The emission tests mentioned in Chapter 4.6.1 were analyzed according to ISO 14644-14. This included:

- The course of particle emissions at each measuring point over time
- Classification of the various measuring points according to ISO 14644-1 with mean and maximum particle emission values

4.6.5 Course of particle emissions over time

The following diagrams show the course of particle emissions at each of the measuring points, as well as for the stated particle size channels, over the total testing time required by the qualification test. The measuring interval of 1 min was the same for all tests. This equates to a test volume of cubic foot (cft).

4.6.5.1 *TP01 inside*

Occurrence of contamination over time:

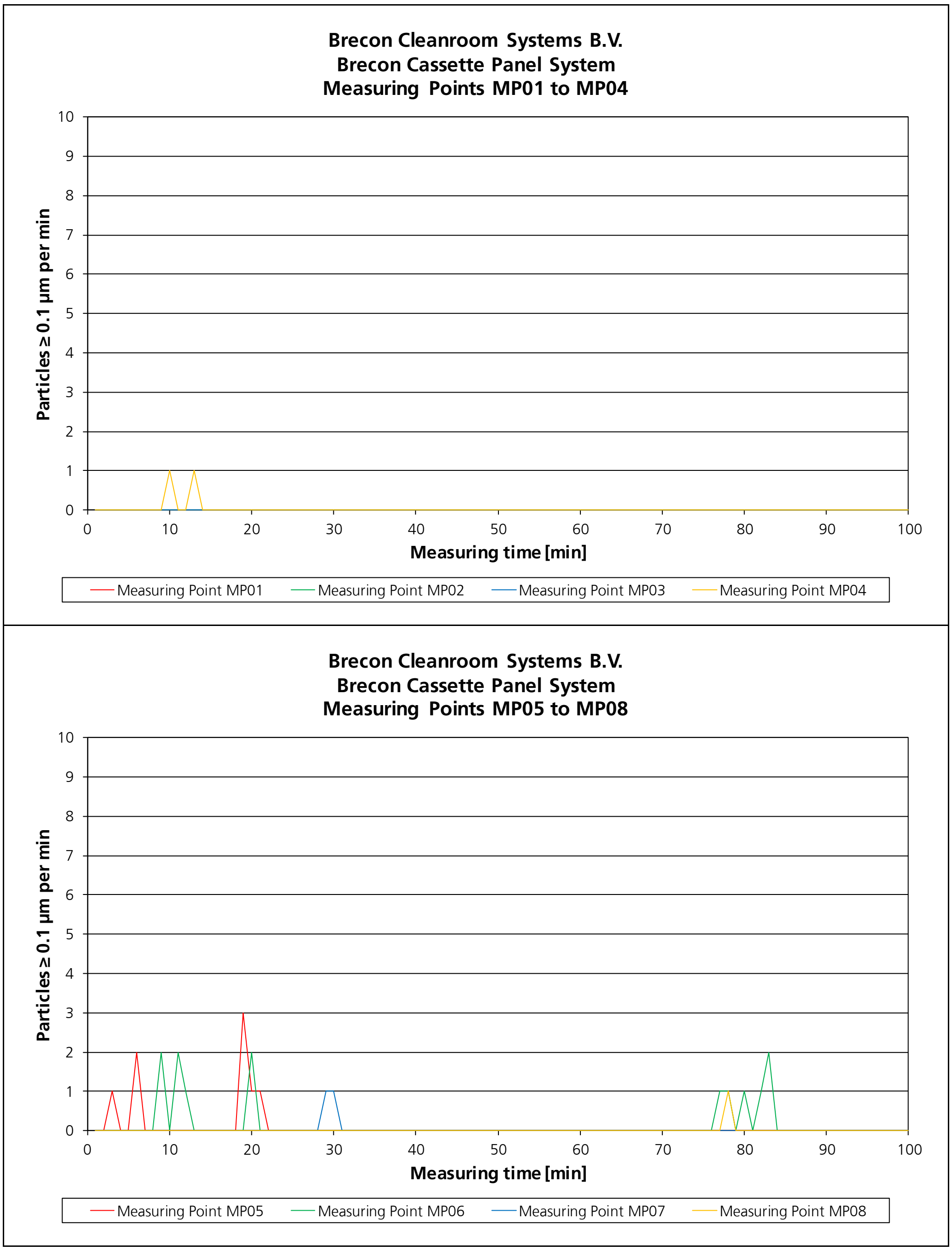


Figure 19 Course of the emission of airborne particles
≥ 0.1 µm over time from the test piece at measuring points MP01 to MP08 over the period of 100 minutes

Fraunhofer IPA

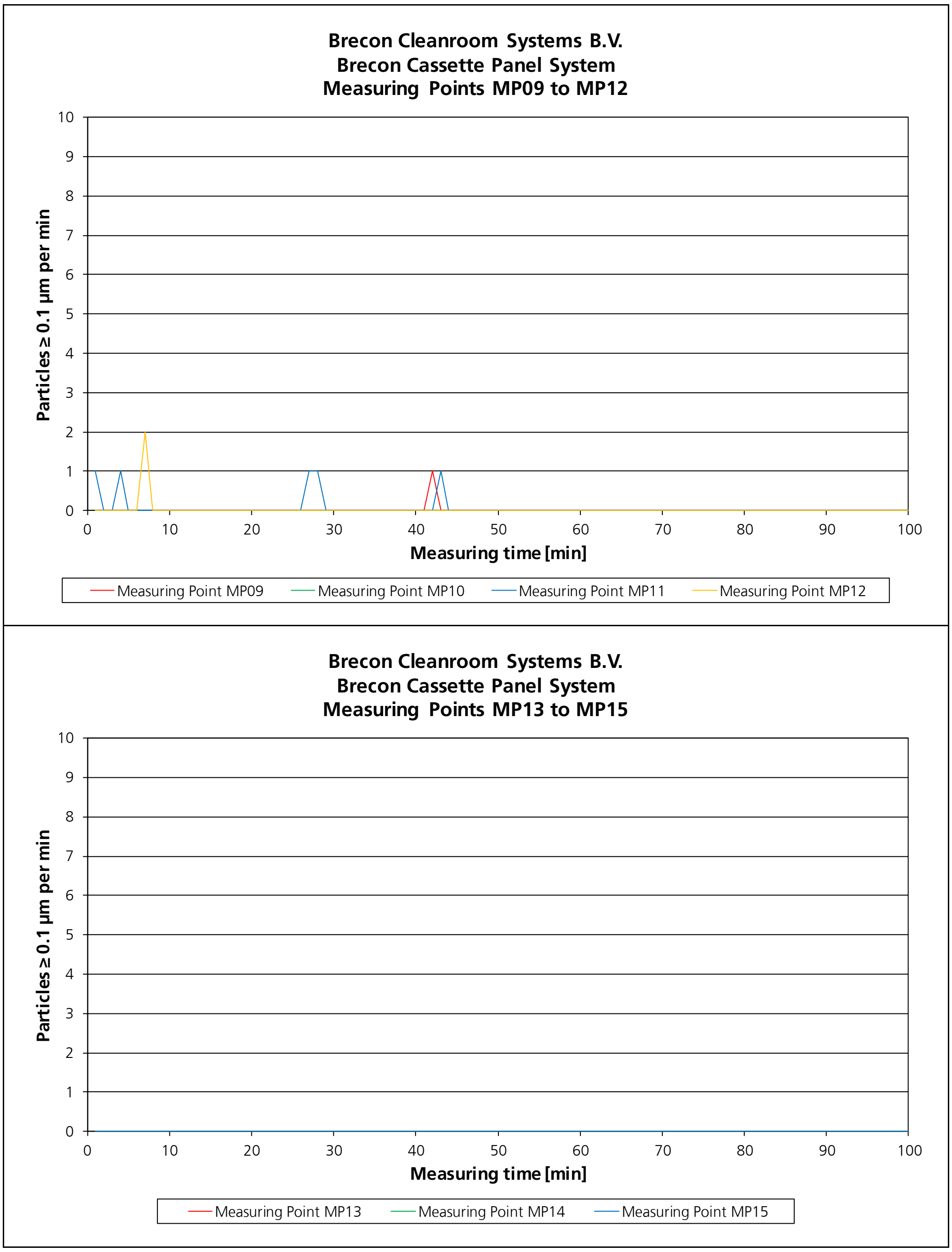


Figure 20 Course of the emission of airborne particles
≥ 0.1 µm over time from the test piece at measuring points MP09 to MP15 over the period of 100 minutes

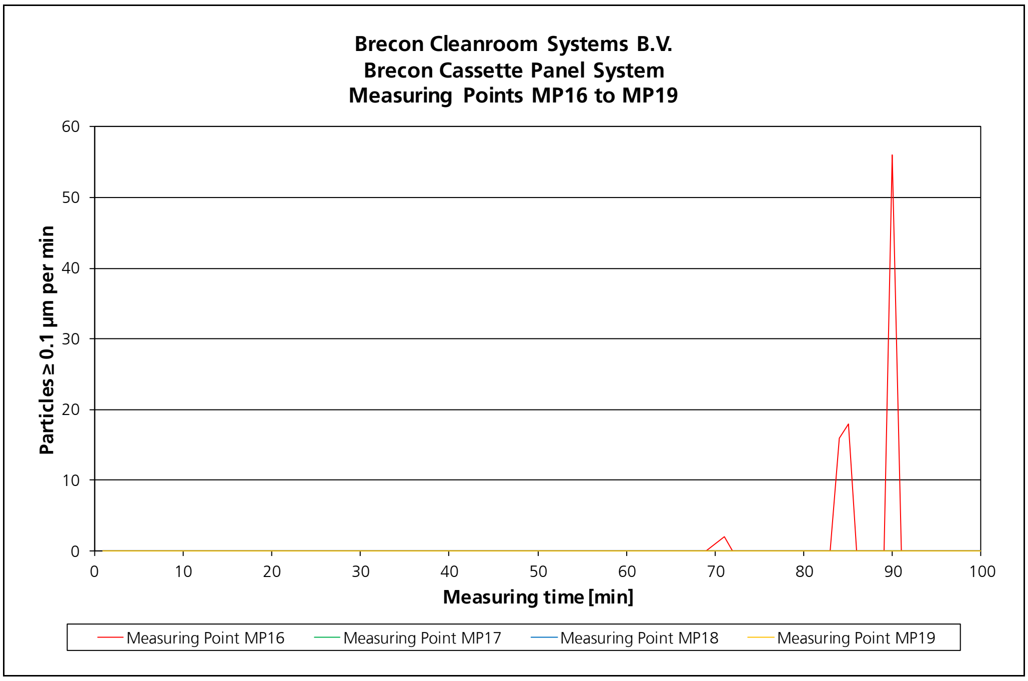


Figure 21 Course of the emission of airborne particles ≥ 0.1 µm over time from the test piece at measuring points MP16 to MP19 over the period of 100 minutes

4.6.5.2 TP01 outside

Occurrence of contamination over time:

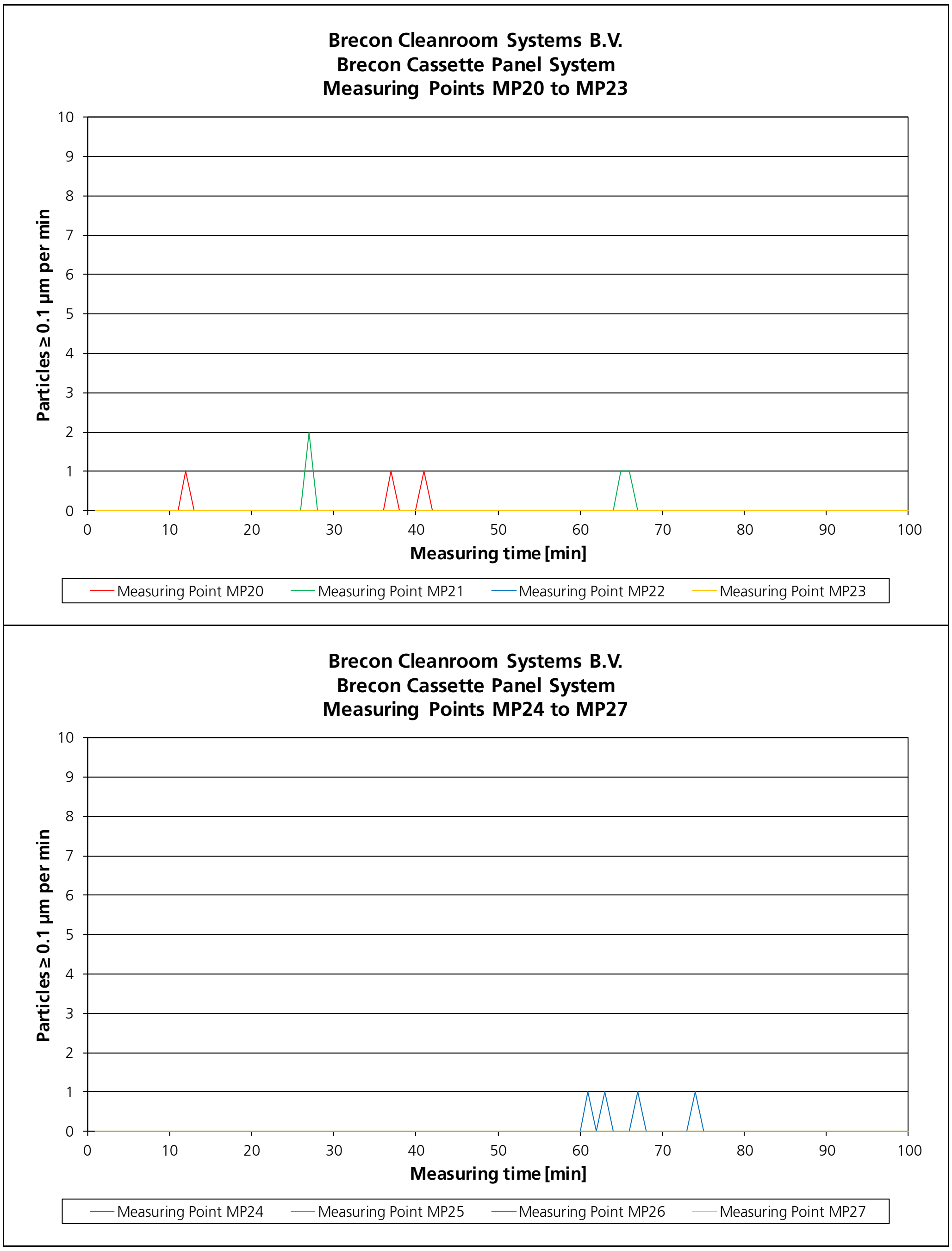


Figure 22 Course of the emission of airborne particles
≥ 0.1 µm over time from the test piece at measuring points MP20 to MP27 over the period of 100 minutes

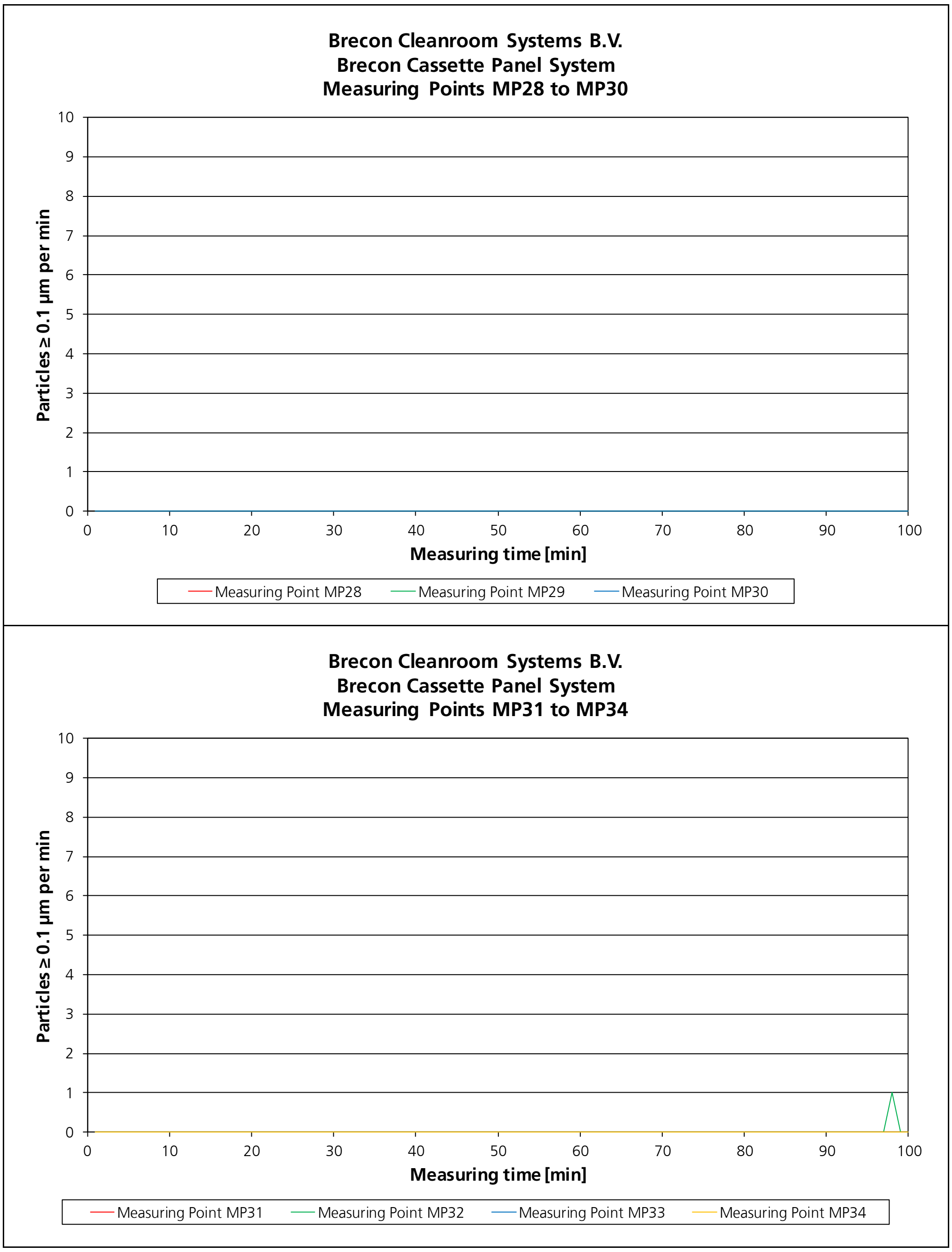


Figure 23 Course of the emission of airborne particles ≥ 0.1 µm over time from the test piece at measuring points MP28 to MP34 over the period of 100 minutes

4.7 Classification

The aim of the tests was to ascertain to what extent the test piece may be operated in clean environments. For this, based on the procedure described in the guideline "Assessment of suitability for use of equipment by airborne particle concentration ISO 14644-14", the empirically-calculated measurement values were analyzed statistically and assessed according to the class limits stated in ISO 14644-1.

4.7.1 Statistical verification of the test results

International standards defining air cleanliness, such as ISO 14644-1, state limit values for the air cleanliness classes that are defined in the respective norm. These limit values are set for a specific number of particle size channels (e.g. ≥ 0.1 µm, ≥ 0.2 µm, ≥ 0.3 µm, ≥ 0.5 µm, ≥ 1.0 µm and ≥ 5.0 µm). When comparing empirically-derived values (e.g. from a qualification test) with such limit values, a certain degree of certainty is required by which the limit value may not be exceeded.

When classifying operating utilities, the standard deviation and mean values are calculated from the measurement values obtained. ISO 14644-14 describes a method which correlates these values with the limit values stated in ISO 14644-1. If a test piece is declared suitable for different classes, the assessment of the test piece is based on the highest class (worst-case assumption).

Fraunhofer IPA

4.7.2 Mean and maximum particle emission values and classification

The following tables show the respective maximum values and arithmetical mean values of particle emissions recorded at the corresponding measuring points (MP) over the total testing time of 100 minutes. The applicable air cleanliness class according to ISO 14644-1 for each measuring point is highlighted.

4.7.2.1 TP01 inside

Brecon Cleanroom Systems B.V. Brecon Cassette Panel System Measuring Points MP01 to MP04					
Statistical parameters		Measuring Point			
		MP01	MP02	MP03	MP04
Mean value for the detection size [particles / cft]	0.1 µm	0.0	0.0	0.0	0.0
	0.2 µm	0.0	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Standard deviation for the detection size [particles / cft]	0.1 µm	0.0	0.0	0.0	0.1
	0.2 µm	0.0	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Air Cleanliness Class [ISO 14644-1]		**1**	**1**	**1**	**1**
Maximum value for the detection size [particles / cft]	0.1 µm	0	0	0	1
	0.2 µm	0	0	0	0
	0.3 µm	0	0	0	0
	0.5 µm	0	0	0	0
	1.0 µm	0	0	0	0
	5.0 µm	0	0	0	0
Minimum value for the detection size [particles / cft]	0.1 µm	0	0	0	0
	0.2 µm	0	0	0	0
	0.3 µm	0	0	0	0
	0.5 µm	0	0	0	0
	1.0 µm	0	0	0	0
	5.0 µm	0	0	0	0

Figure 24 Statistical characteristics of the measuring points MP01 to MP04

Fraunhofer IPA

Brecon Cleanroom Systems B.V. Brecon Cassette Panel System Measuring Points MP05 to MP08					
Statistical parameters		Measuring Point			
		MP05	MP06	MP07	MP08
Mean value for the detection size [particles / cft]	0.1 µm	0.1	0.1	0.0	0.0
	0.2 µm	0.0	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Standard deviation for the detection size [particles / cft]	0.1 µm	0.4	0.4	0.1	0.1
	0.2 µm	0.2	0.1	0.0	0.0
	0.3 µm	0.2	0.1	0.0	0.0
	0.5 µm	0.0	0.1	0.0	0.0
	1.0 µm	0.0	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Air Cleanliness Class [ISO 14644-1]		**2**	**2**	**1**	**1**
Maximum value for the detection size [particles / cft]	0.1 µm	3	2	1	1
	0.2 µm	2	1	0	0
	0.3 µm	2	1	0	0
	0.5 µm	0	1	0	0
	1.0 µm	0	0	0	0
	5.0 µm	0	0	0	0
Minimum value for the detection size [particles / cft]	0.1 µm	0	0	0	0
	0.2 µm	0	0	0	0
	0.3 µm	0	0	0	0
	0.5 µm	0	0	0	0
	1.0 µm	0	0	0	0
	5.0 µm	0	0	0	0

Figure 25 Statistical characteristics of the measuring points MP05 to MP08

Fraunhofer IPA

Brecon Cleanroom Systems B.V. Brecon Cassette Panel System Measuring Points MP09 to MP12					
Statistical parameters		Measuring Point			
		MP09	MP10	MP11	MP12
Mean value for the detection size [particles / cft]	0.1 µm	0.0	0.0	0.1	0.0
	0.2 µm	0.0	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Standard deviation for the detection size [particles / cft]	0.1 µm	0.1	0.0	0.2	0.2
	0.2 µm	0.0	0.0	0.0	0.2
	0.3 µm	0.0	0.0	0.0	0.1
	0.5 µm	0.0	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Air Cleanliness Class [ISO 14644-1]		**1**	**1**	**1**	**1**
Maximum value for the detection size [particles / cft]	0.1 µm	1	0	1	2
	0.2 µm	0	0	0	2
	0.3 µm	0	0	0	1
	0.5 µm	0	0	0	0
	1.0 µm	0	0	0	0
	5.0 µm	0	0	0	0
Minimum value for the detection size [particles / cft]	0.1 µm	0	0	0	0
	0.2 µm	0	0	0	0
	0.3 µm	0	0	0	0
	0.5 µm	0	0	0	0
	1.0 µm	0	0	0	0
	5.0 µm	0	0	0	0

Figure 26 Statistical characteristics of the measuring points MP09 to MP12

Brecon Cleanroom Systems B.V. Brecon Cassette Panel System Measuring Points MP13 to MP15				
Statistical parameters		Measuring Point		
		MP13	MP14	MP15
Mean value for the detection size [particles / cft]	0.1 µm	0.0	0.0	0.0
	0.2 µm	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0
Standard deviation for the detection size [particles / cft]	0.1 µm	0.0	0.0	0.0
	0.2 µm	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0
Air Cleanliness Class [ISO 14644-1]		**1**	**1**	**1**
Maximum value for the detection size [particles / cft]	0.1 µm	0	0	0
	0.2 µm	0	0	0
	0.3 µm	0	0	0
	0.5 µm	0	0	0
	1.0 µm	0	0	0
	5.0 µm	0	0	0
Minimum value for the detection size [particles / cft]	0.1 µm	0	0	0
	0.2 µm	0	0	0
	0.3 µm	0	0	0
	0.5 µm	0	0	0
	1.0 µm	0	0	0
	5.0 µm	0	0	0

Figure 27 Statistical characteristics of the measuring points MP13 to MP15

Brecon Cleanroom Systems B.V. Brecon Cassette Panel System Measuring Points MP16 to MP19					
Statistical parameters		Measuring Point			
		MP16	MP17	MP18	MP19
Mean value for the detection size [particles / cft]	0.1 µm	0.9	0.0	0.0	0.0
	0.2 µm	0.1	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Standard deviation for the detection size [particles / cft]	0.1 µm	6.1	0.0	0.0	0.0
	0.2 µm	0.3	0.0	0.0	0.0
	0.3 µm	0.1	0.0	0.0	0.0
	0.5 µm	0.1	0.0	0.0	0.0
	1.0 µm	0.1	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Air Cleanliness Class [ISO 14644-1]		**3**	**1**	**1**	**1**
Maximum value for the detection size [particles / cft]	0.1 µm	56	0	0	0
	0.2 µm	2	0	0	0
	0.3 µm	1	0	0	0
	0.5 µm	1	0	0	0
	1.0 µm	1	0	0	0
	5.0 µm	0	0	0	0
Minimum value for the detection size [particles / cft]	0.1 µm	0	0	0	0
	0.2 µm	0	0	0	0
	0.3 µm	0	0	0	0
	0.5 µm	0	0	0	0
	1.0 µm	0	0	0	0
	5.0 µm	0	0	0	0

Figure 28 Statistical characteristics of the measuring points MP16 to MP19

From the respective calculations for the detection sizes ≥ 0.1 µm, ≥ 0.2 µm, ≥ 0.3 µm, ≥ 0.5 µm, ≥ 1.0 µm and ≥ 5.0 µm, it can be derived that the test piece is suitable for use in **ISO Class 3** cleanrooms according to ISO 14644-1.

4.7.2.2 *TP01 outside*

Brecon Cleanroom Systems B.V. Brecon Cassette Panel System Measuring Points MP20 to MP23					
Statistical parameters		Measuring Point			
		MP20	MP21	MP22	MP23
Mean value for the detection size [particles / cft]	0.1 µm	0.0	0.0	0.0	0.0
	0.2 µm	0.0	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Standard deviation for the detection size [particles / cft]	0.1 µm	0.2	0.2	0.0	0.0
	0.2 µm	0.0	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Air Cleanliness Class [ISO 14644-1]		**1**	**1**	**1**	**1**
Maximum value for the detection size [particles / cft]	0.1 µm	1	2	0	0
	0.2 µm	0	0	0	0
	0.3 µm	0	0	0	0
	0.5 µm	0	0	0	0
	1.0 µm	0	0	0	0
	5.0 µm	0	0	0	0
Minimum value for the detection size [particles / cft]	0.1 µm	0	0	0	0
	0.2 µm	0	0	0	0
	0.3 µm	0	0	0	0
	0.5 µm	0	0	0	0
	1.0 µm	0	0	0	0
	5.0 µm	0	0	0	0

Figure 29 Statistical characteristics of the measuring points MP20 to MP23

Fraunhofer IPA

Brecon Cleanroom Systems B.V. Brecon Cassette Panel System Measuring Points MP24 to MP27					
Statistical parameters		Measuring Point			
		MP24	MP25	MP26	MP27
Mean value for the detection size [particles / cft]	0.1 µm	0.0	0.0	0.0	0.0
	0.2 µm	0.0	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Standard deviation for the detection size [particles / cft]	0.1 µm	0.0	0.0	0.2	0.0
	0.2 µm	0.0	0.0	0.1	0.0
	0.3 µm	0.0	0.0	0.1	0.0
	0.5 µm	0.0	0.0	0.1	0.0
	1.0 µm	0.0	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Air Cleanliness Class [ISO 14644-1]		**1**	**1**	**1**	**1**
Maximum value for the detection size [particles / cft]	0.1 µm	0	0	1	0
	0.2 µm	0	0	1	0
	0.3 µm	0	0	1	0
	0.5 µm	0	0	1	0
	1.0 µm	0	0	0	0
	5.0 µm	0	0	0	0
Minimum value for the detection size [particles / cft]	0.1 µm	0	0	0	0
	0.2 µm	0	0	0	0
	0.3 µm	0	0	0	0
	0.5 µm	0	0	0	0
	1.0 µm	0	0	0	0
	5.0 µm	0	0	0	0

Figure 30 Statistical characteristics of the measuring points MP24 to MP27

Fraunhofer IPA

Brecon Cleanroom Systems B.V. Brecon Cassette Panel System Measuring Points MP28 to MP30				
Statistical parameters		Measuring Point		
		MP28	MP29	MP30
Mean value for the detection size [particles / cft]	0.1 µm	0.0	0.0	0.0
	0.2 µm	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0
Standard deviation for the detection size [particles / cft]	0.1 µm	0.0	0.0	0.0
	0.2 µm	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0
Air Cleanliness Class [ISO 14644-1]		**1**	**1**	**1**
Maximum value for the detection size [particles / cft]	0.1 µm	0	0	0
	0.2 µm	0	0	0
	0.3 µm	0	0	0
	0.5 µm	0	0	0
	1.0 µm	0	0	0
	5.0 µm	0	0	0
Minimum value for the detection size [particles / cft]	0.1 µm	0	0	0
	0.2 µm	0	0	0
	0.3 µm	0	0	0
	0.5 µm	0	0	0
	1.0 µm	0	0	0
	5.0 µm	0	0	0

Figure 31 Statistical characteristics of the measuring points MP28 to MP30

Fraunhofer IPA

Brecon Cleanroom Systems B.V. Brecon Cassette Panel System Measuring Points MP31 to MP34					
Statistical parameters		Measuring Point			
		MP31	MP32	MP33	MP34
Mean value for the detection size [particles / cft]	0.1 µm	0.0	0.0	0.0	0.0
	0.2 µm	0.0	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Standard deviation for the detection size [particles / cft]	0.1 µm	0.0	0.1	0.0	0.0
	0.2 µm	0.0	0.0	0.0	0.0
	0.3 µm	0.0	0.0	0.0	0.0
	0.5 µm	0.0	0.0	0.0	0.0
	1.0 µm	0.0	0.0	0.0	0.0
	5.0 µm	0.0	0.0	0.0	0.0
Air Cleanliness Class [ISO 14644-1]		**1**	**1**	**1**	**1**
Maximum value for the detection size [particles / cft]	0.1 µm	0	1	0	0
	0.2 µm	0	0	0	0
	0.3 µm	0	0	0	0
	0.5 µm	0	0	0	0
	1.0 µm	0	0	0	0
	5.0 µm	0	0	0	0
Minimum value for the detection size [particles / cft]	0.1 µm	0	0	0	0
	0.2 µm	0	0	0	0
	0.3 µm	0	0	0	0
	0.5 µm	0	0	0	0
	1.0 µm	0	0	0	0
	5.0 µm	0	0	0	0

Figure 32 Statistical characteristics of the measuring points MP31 to MP34

From the respective calculations for the detection sizes ≥ 0.1 µm, ≥ 0.2 µm, ≥ 0.3 µm, ≥ 0.5 µm, ≥ 1.0 µm and ≥ 5.0 µm, it can be derived that the test piece is suitable for use in **ISO Class 1** cleanrooms according to ISO 14644-1.

4.8 Summary of the classification results

The following table gives an overview of the classification of the various measuring points MP01 to MP34:

Brecon Cassette Panel System manufactured by **Brecon Cleanroom Systems B.V. - inside**					
Granite Standard Coil Coated Steel					
Measuring Point	MP01	MP02	MP03	MP04	MP05
Air Cleanliness Class (according to ISO 14644-1)	1	1	1	1	2
Measuring Point	MP06	MP07	MP08	MP09	MP10
Air Cleanliness Class (according to ISO 14644-1)	2	1	1	1	1
Measuring Point	MP11	MP12	MP13	MP14	
Air Cleanliness Class (according to ISO 14644-1)	1	1	1	1	
Formica High Pressure Laminate					
Measuring Point	MP15	**MP16**	MP17	MP18	MP19
Air Cleanliness Class (according to ISO 14644-1)	1	**3**	1	1	1

Figure 33 Overall classification of Brecon Cassette Panel System - innside

Brecon Cassette Panel System manufactured by **m Brecon Cleanroom Systems B.V.- outside**					
Granite Standard Coil Coated Steel					
Measuring Point	MP20	MP21	MP22	MP23	MP24
Air Cleanliness Class (according to ISO 14644-1)	1	1	1	1	1
Measuring Point	MP25	MP26	MP27	MP28	MP29
Air Cleanliness Class (according to ISO 14644-1)	1	1	1	1	1
Measuring Point	MP30				
Air Cleanliness Class (according to ISO 14644-1)	1				
Formica High Pressure Laminate					
Measuring Point	MP31	MP32	MP33	MP34	
Air Cleanliness Class (according to ISO 14644-1)	1	1	1	1	

Figure 34 Overall classification of Brecon Cassette Panel System- outside

From the calculations of the probability of exceeding limiting values for the detection sizes ≥ 0.1 µm, ≥ 0.2 µm, ≥ 0.3 µm, ≥ 0.5 µm, ≥ 1.0 µm and ≥ 5.0 µm, it can be derived that the **Brecon Cassette Panel System** manufactured by m **Brecon Cleanroom Systems B.V.** is suitable for use in cleanrooms fulfilling the specifications of **ISO Class 3** in accordance with ISO 14644-1 when operated with the specified parameters.

It must be pointed out, that according to ISO 14644-1 cleanrooms classes 1 to 5 have a high filter occupancy, with the result that large-surface ceiling systems cannot be used in some cases. Cleanrooms with a horizontal displacement flow form an exception to this. Particle emission behavior should be re-assessed in the respective assembly situation.

4.9 Annex: comparison of different classifications of airborne particulate contamination

In the following table, the limit values defining air cleanliness classes according to the international standard **ISO 14644-1** are compared with the limit values stated in **EG GMP Guideline** Volume 4 Annex 1 and in the American norm **US Federal Standard 209E** (retracted). The comparison concerns the particle size channels stated explicitly in ISO 14644-1; limit values are stated for the reference volumes of 1 m^3 and 1 cft (1 cubic foot = 0.0283 m^3).

Regulatory				Limiting values of each Air Cleanliness Class for differing particle sizes and reference volumes (acc. to ISO 14644-1)											
EG-GMP "in operation"	EG-GMP "at rest"	US Fed. Standard 209E*	DIN EN ISO 14644-1	0.1 µm		0.2 µm		0.3 µm		0.5 µm		1.0 µm		5.0 µm	
				per [m^3]	per [cbf]	per [m^3]	per [cbf]	per [m^3]	per [cbf]	per [m^3]	per [cbf]	per [m^3]	per [cbf]	per [m^3]	per [cbf]
			1	10	0,3										
			2	100	3	24	1	10	0,3						
			3	1,000	30	237	7	102	3	35	1				
		1		1,240	35	265	8	106	3	35	1				
			4	10,000	300	2,370	67	1,020	29	352	9,9	83	2		
		10		12,000	340	2,650	75	1,060	29	353	10				
			5	100,000	2,833	23,700	671	10,200	289	3,520	100	832	24		
	A									3,520	100			20	0,6
A										3,520	100			20	0,6
	B									3,520	100			29	0,8
		100				26,500	750	10,600	300	3,530	100				
			6	1,000,000	28,329	237,000	6,710	102,000	2,890	35,200	997	8,320	235	293	8
		1,000								35,300	1,000			247	7
			7							352,000	9,972	83,200	2,357	2,930	83
B										352,000	9,972			2,900	82
	C									352,000	9,972			2,900	82
		10,000								353,000	10,000			2,470	70
			8							3,520,000	99,716	832,000	23,569	29,300	830
C										3,520,000	99,716			29,000	821
	D									3,520,000	99,716			29,000	821
		100,000								3,530,000	100,000			24,700	700
			9							35,200,000	997,167	8,320,000	235,694	29,3000	8,300

Figure 35 Overview of limit values for airborne particles per m^3 or cft for the standards ISO 14644-1, EU GMP Guideline Volume 4, Annex 1 and US Federal Standard 209E (retracted)

Although limit values are stated for tests on **biotic** airborne particles in EU GMP Guideline Volume 4, Annex 1, this does not form part of the qualification tests conducted at Fraunhofer IPA. Since all manufacturing environments have their own individual germ spectrum, these tests cannot be conducted in a reference laboratory and therefore need to be performed in the respective manufacturing environment. The individual germ spectrum and magnitude of microbial loads are decisively influenced by the production processes, the environment and operating staff in the relevant production areas.

5 Determination of resistance to chemicals

5.1 Test conditions

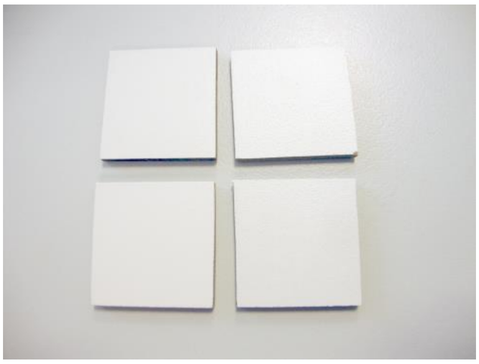
Chemical resistance tests show to what extent the materials under investigation may be used in a clean manufacturing environment. Among other things, the materials must be resistant to cleaning-, process- and disinfection-reagents.

The tests were carried out in accordance with the procedure laid down in ISO 2812-1 ("Determination of resistance to liquids – Part 1: Immersion in liquids other than water") for TP02 and ISO 2812-4 ("Determination of resistance to liquids – droplet/spot test") for TP03.

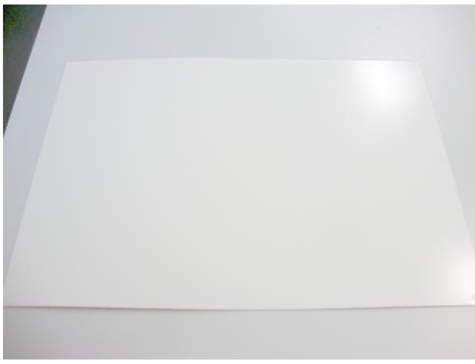
The chemical resistance was tested against 10 typical reagents.

5.2 Analyzed sample

The following samples were analyzed for chemical resistance:



TP02



TP03

Figure 36 Analyzed samples

5.3 Test procedure

In the chemical resistance tests, the material samples were subjected to a defined stress using the test chemicals.

The immersion test is carried out in accordance with ISO 2812-1.

With the immersion test, a complete material sample is placed in a receptacle filled with the test chemical and then hermetically sealed.

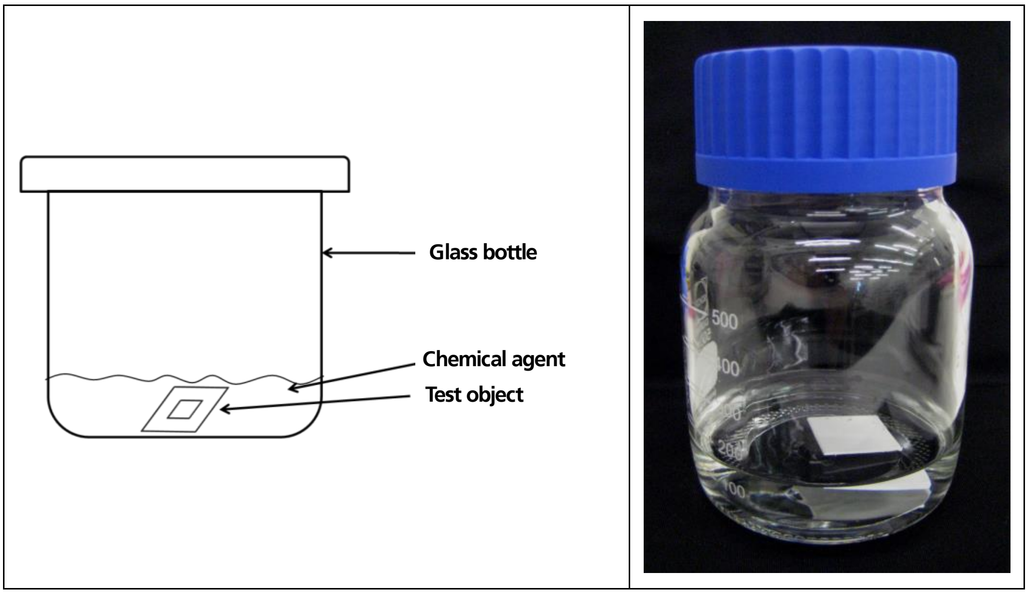


Figure 37 Diagrammatic sketch: Immersion of the test sample into the chemical (left)
Test set-up: Immersion of the test sample into the chemical (right)

With the spot test, the test chemical is filled in receptacle of glass with a port diameter of nearly 50 mm. Then the cup is covered with a gasket and the test surface. This configuration is fixed in a test gear and closed hermetically. After then the configuration is rotated by 180°, so that the chemical get in contact with the test surface.

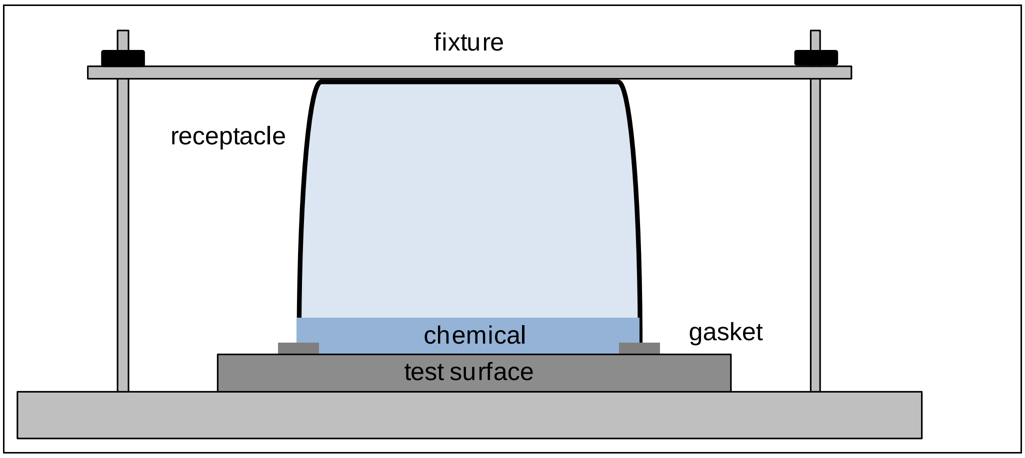


Figure 38 Diagrammatic sketch: application of the chemicals using the spot test

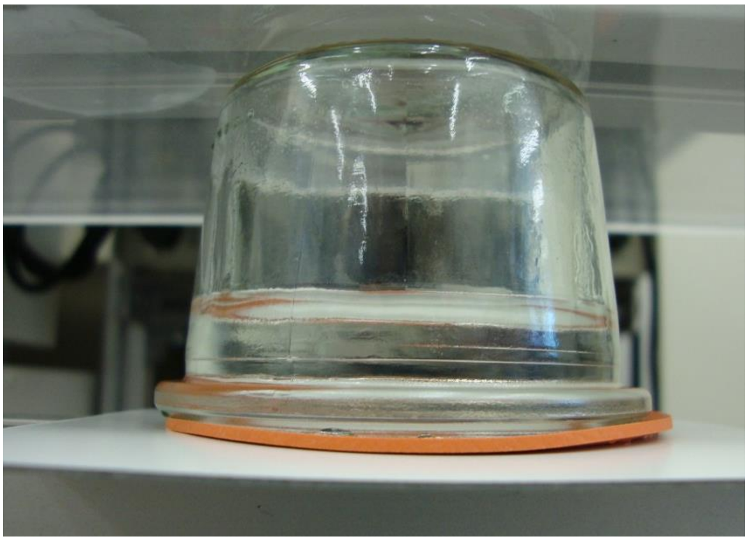


Figure 39 Test set-up for spot test

The test samples were subjected to each reagent for a period of one (1), three (3), six (6) and 24 hours and then examined for visible alterations.

On completion of the stress period, the test chemical was wiped off the test surface with a cleanroom cloth and inspected. The sample was reassessed after one hour to see if further alterations had taken place or if any alterations had lessened.

5.4 Assessment criteria

The test area was visually assessed in accordance with ISO 4628-1 (Evaluation of degradation of coatings - Designation of quantity and size of defects, and of intensity of uniform changes in appearance – Part 1: General introduction and designation system) and VDI 2083 Part 17. Increases with a factor 10 and with regard to the following criteria:

- Type of damage (alteration in degree of shine, discoloration or yellowing, swelling, softening or altered resistance to scratching, any other noticeable alterations)
- Amount of damage (N-values)
- Size of damage (S-values)
- Intensity of alteration (I-values)

5.4.1 Assessment of the amount of damage

The amount of damage to the coating, occurring in the form of irregularities or localized flaws in the coating which are irregularly distributed or only in specific places, is assessed according to the following table.

Value	Amount of damage
N0	No recognizable damage
N1	Very little, i.e. small, just recognizable amounts of damage
N2	Little, but significant amounts of damage
N3	Average amount of damage
N4	Severe amounts of damage
N5	Extreme amounts of damage

Figure 40 Criteria for assessing the amount of damage

5.4.2 Assessment of the size of damage

The average size of damage – if it makes sense – is assessed according to the following table.

Value	Size of damage
S0	Not visible on 10x magnification
S1	Only visible on 10x magnification
S2	Just visible with the naked eye
S3	Clearly visible up to 0.5 mm
S4	Area 0.5-5 mm
S5	Larger than 5 mm

Figure 41 Criteria for assessing the size of damage

5.4.3 Assessment of the intensity of alteration

The intensity of uniform alterations in the appearance of a coating such as changes in colour, e.g. yellowing, is assessed according to the following table

Value	Intensity of alteration
I0	Unchanged, no recognizable alteration
I1	Very slight, just recognizable alteration
I2	Slight, clearly recognizable alteration
I3	Average, clearly recognizable up to 0.5 mm
I4	Severe alteration
I5	Extreme alteration

Figure 42 Criteria for assessing the intensity of alteration

The analysis is made as follows:

"Blistering, N2-S2" or "Discoloration, I1"

Any other noticeable irregularities are also documented.

5.4.4 Reagents utilized

To simulate stress on the material samples due to cleaning-, process- and disinfection-agents, the following reagents were used:

- Formalin (37 %)
- Ammoniac (25 %)
- Hydrogen peroxide (30 %)
- Sulfuric acid (5 %)
- Phosphoric acid (30 %)
- Peracetic acid (15 %)
- Hydrochloric acid (5 %)
- Isopropanol (100 %)
- Sodium hydroxide (5 %)
- Sodium hypochlorite (5 %)

5.4.5 Microscopic assessment

The microscopic assessment was made by a Zeiss stereo magnifier and a color camera AxioCam HRc with 10x magnification.

5.4.6 Classification according to VDI 2083 Part 17

The average of each worst value (N, S, I) after 24 hours of incubation of all ten tested chemicals gives the classification value according to the following chart:

Reference number (obtained average)	Classification
0	excellent
1	very good
2	good
3	weak
4	very weak
5	none

Figure 43 Classification according to VDI 2083 Part 17

5.5 Results of the chemical resistance tests TP02

A table has been selected to document the test results in order to show the chemical resistance of the test surfaces to the reagents. All images were recorded using a Zeiss stereo magnifier, colour camera and a coaxial illumination. Identical settings were used to record all images in order to enable a direct comparison to be made.

5.5.1 Formalin 37 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		NO
3 h		NO
6 h		NO
24 h		**NO**

Figure 44 TP02 subjected to formalin 37 %

The results show that the chemical resistance of the TP02 to **formalin 37 %** is **excellent**.

5.5.2 Ammoniac 25 %

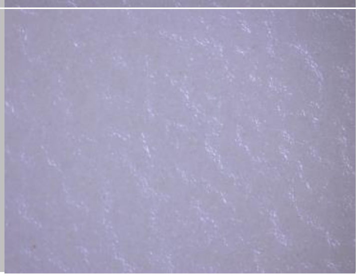
Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		NO
3 h		NO
6 h		NO
24 h		**NO**

Figure 45 TP02 subjected to ammoniac 25 %

The results show that the chemical resistance of the TP02 to **ammoniac 25 %** is **excellent**.

5.5.3 Hydrogen peroxide 30 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		NO
3 h		NO
6 h		NO
24 h		**NO**

Figure 46 TP02 subjected to hydrogen peroxide 30 %

The results show that the chemical resistance of the TP02 to **hydrogen peroxide 30 %** is **excellent**.

5.5.4 Sulfuric acid 5 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		NO
3 h		NO
6 h		NO
24 h		**NO**

Figure 47 TP02 subjected to sulfuric acid 5 %

The results show that the chemical resistance of the TP02 to **sulfuric acid 5 %** is **excellent**.

5.5.5 Phosphoric acid 30 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		N0
3 h		N0
6 h		Changes of surface I1
24 h		**Changes of surface I1**

Figure 48 TP02 subjected to phosphoric acid 30 %

The results show that the chemical resistance of the TP02 to **phosphoric acid 30 %** is **very good**.

5.5.6 Peracetic acid 15 %

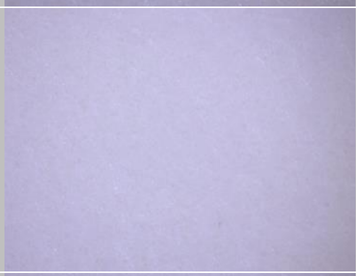
Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		N0
3 h		N0
6 h		Changes of surface I1
24 h		**Changes of surface I1**

Figure 49 TP02 subjected to peracetic acid 15 %

The results show that the chemical resistance of the TP02 to **peracetic acid 15 %** is **very good**.

5.5.7 Hydrochloric acid 5 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		NO
3 h		NO
6 h		NO
24 h		**NO**

Figure 50 TP02 subjected to hydrochloric acid 5 %

The results show that the chemical resistance of the TP02 to **hydrochloric acid 5 %** is **excellent**.

5.5.8 Isopropanol 100 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		NO
3 h		NO
6 h		NO
24 h		**NO**

Figure 51 TP02 subjected to isopropanol 100 %

The results show that the chemical resistance of the TP02 to **isopropanol 100 %** is **excellent**.

5.5.9 Sodium hydroxide 5 %

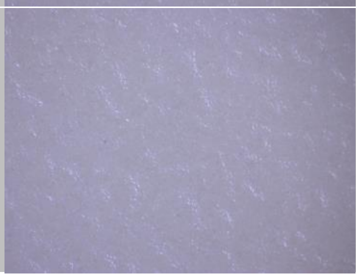
Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		N0
3 h		N0
6 h		N0
24 h		**N0**

Figure 52 TP02 subjected to sodium hydroxide 5 %

The results show that the chemical resistance of the TP02 to **sodium hydroxide 5 %** is **excellent**.

5.5.10 Sodium hypochlorite 5 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		NO
3 h		NO
6 h		NO
24 h		**NO**

Figure 53 TP02 subjected to sodium hypochlorite 5 %

The results show that the chemical resistance of the TP02 to **sodium hypochlorite 5 %** is **excellent**.

5.6 Results of the chemical resistance tests TP03

A table has been selected to document the test results in order to show the chemical resistance of the test surfaces to the reagents. All images were recorded using a Zeiss stereo magnifier, colour camera and a coaxial illumination. Identical settings were used to record all images in order to enable a direct comparison to be made.

5.6.1 Formalin 37 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		NO
3 h		NO
6 h		NO
24 h		**NO**

Figure 54 TP03 subjected to formalin 37 %

The results show that the chemical resistance of the TP03 to **formalin 37 %** is **excellent**.

5.6.2 Ammoniac 25 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		NO
3 h		NO
6 h		NO
24 h		**NO**

Figure 55 TP03 subjected to ammoniac 25 %

The results show that the chemical resistance of the TP03 to **ammoniac 25 %** is **excellent**.

5.6.3 Hydrogen peroxide 30 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		NO
3 h		NO
6 h		NO
24 h		**NO**

Figure 56 TP03 subjected to hydrogen peroxide 30 %

The results show that the chemical resistance of the TP03 to **hydrogen peroxide 30 %** is **excellent**.

5.6.4 Sulfuric acid 5 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		N0
3 h		N0
6 h		N0
24 h		**N0**

Figure 57 TP03 subjected to sulfuric acid 5 %

The results show that the chemical resistance of the TP03 to **sulfuric acid 5 %** is **excellent**.

5.6.5 Phosphoric acid 30 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		N0
3 h		N0
6 h		N0
24 h		**N0**

Figure 58 TP03 subjected to phosphoric acid 30 %

The results show that the chemical resistance of the TP03 to **phosphoric acid 30 %** is **excellent**.

5.6.6 Peracetic acid 15 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		Discoloring I1
3 h		Blistering N4S4
6 h		Blistering N5S5
24 h		**Blistering N5S5**

Figure 59 TP03 subjected to peracetic acid 15 %

The results show that the chemical resistance of the TP03 to **peracetic acid 15 %** is **none**.

5.6.7 Hydrochloric acid 5 %

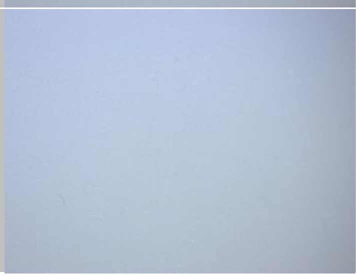
Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		N0
3 h		N0
6 h		N0
24 h		**N0**

Figure 60 TP03 subjected to hydrochloric acid 5 %

The results show that the chemical resistance of the TP03 to **hydrochloric acid 5 %** is **excellent**.

5.6.8 Isopropanol 100 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		Discoloring I1
3 h		Discoloring I1
6 h		Discoloring I1
24 h		**Discoloring I1**

Figure 61 TP03 subjected to isopropanol 100 %

The results show that the chemical resistance of the TP03 to **isopropanol 100 %** is **very good**.

5.6.9 Sodium hydroxide 5 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		N0
3 h		N0
6 h		N0
24 h		**N0**

Figure 62 TP03 subjected to sodium hydroxide 5 %

The results show that the chemical resistance of the TP03 to **sodium hydroxide 5 %** is **excellent**.

5.6.10 Sodium hypochlorite 5 %

Time	Microscopic image 10x magnification	Value
Blank value		Before testing
1 h		NO
3 h		NO
6 h		NO
24 h		**NO**

Figure 63 TP03 subjected to sodium hypochlorite 5 %

The results show that the chemical resistance of the TP03 to **sodium hypochlorite 5 %** is **excellent**.

5.7 Summary of results of the chemical resistance tests

TP02

The following tables give an overall assessment of the material sample:

Chemicals	Incubation			
	1 h	3 h	6 h	**24 h**
Formalin 37 %	N0	N0	N0	**N0**
Ammoniac 25 %	N0	N0	N0	**N0**
Hydrogen peroxide 30 %	N0	N0	N0	**N0**
Sulfuric acid 5 %	N0	N0	N0	**N0**
Phosphoric acid 30 %	N0	N0	I1	**I1**
Peracetic acid 15 %	N0	N0	I1	**I1**
Hydrochloric acid 5 %	N0	N0	N0	**N0**
Isopropanol 100 %	N0	N0	N0	**N0**
Sodium hydroxide 5 %	N0	N0	N0	**N0**
Sodium hypochlorite 5 %	N0	N0	N0	**N0**

Figure 64 Results of the chemical resistance tests on the material sample shown in the form of a table with corresponding values

Chemicals	Incubation			
	1 h	3 h	6 h	**24 h**
Formalin 37 %	excellent	excellent	excellent	**excellent**
Ammoniac 25 %	excellent	excellent	excellent	**excellent**
Hydrogen peroxide 30 %	excellent	excellent	excellent	**excellent**
Sulfuric acid 5 %	excellent	excellent	excellent	**excellent**
Phosphoric acid 30 %	excellent	excellent	very good	**very good**
Peracetic acid 15 %	excellent	excellent	very good	**very good**
Hydrochloric acid 5 %	excellent	excellent	excellent	**excellent**
Isopropanol 100 %	excellent	excellent	excellent	**excellent**
Sodium hydroxide 5 %	excellent	excellent	excellent	**excellent**
Sodium hypochlorite 5 %	excellent	excellent	excellent	**excellent**

Figure 65 Results of the chemical resistance tests on the material sample shown in the form of a table with the subsequent classification.

TP03

The following tables give an overall assessment of the material sample:

Chemicals	Incubation			
	1 h	3 h	6 h	**24 h**
Formalin 37 %	N0	N0	N0	**N0**
Ammoniac 25 %	N0	N0	N0	**N0**
Hydrogen peroxide 30 %	N0	N0	N0	**N0**
Sulfuric acid 5 %	N0	N0	N0	**N0**
Phosphoric acid 30 %	N0	N0	N0	**N0**
Peracetic acid 15 %	I1	N4S4	N5S5	**N5S5**
Hydrochloric acid 5 %	N0	N0	N0	**N0**
Isopropanol 100 %	I1	I1	I1	**I1**
Sodium hydroxide 5 %	N0	N0	N0	**N0**
Sodium hypochlorite 5 %	N0	N0	N0	**N0**

Figure 66 Results of the chemical resistance tests on the material sample shown in the form of a table with corresponding values

Chemicals	Incubation			
	1 h	3 h	6 h	**24 h**
Formalin 37 %	excellent	excellent	excellent	**excellent**
Ammoniac 25 %	excellent	excellent	excellent	**excellent**
Hydrogen peroxide 30 %	excellent	excellent	excellent	**excellent**
Sulfuric acid 5 %	excellent	excellent	excellent	**excellent**
Phosphoric acid 30 %	excellent	excellent	excellent	**excellent**
Peracetic acid 15 %	very good	very weak	none	**none**
Hydrochloric acid 5 %	excellent	excellent	excellent	**excellent**
Isopropanol 100 %	very good	very good	very good	**very good**
Sodium hydroxide 5 %	excellent	excellent	excellent	**excellent**
Sodium hypochlorite 5 %	excellent	excellent	excellent	**excellent**

Figure 67 Results of the chemical resistance tests on the material sample shown in the form of a table with the subsequent classification.

6 H_2O_2 absorption and desorption behavior

GMP controlled environments for sterile production require regular decontamination in order to minimize the biological burden to an accepted level. The usage of vaporized hydrogen peroxide (H_2O_2) to decontaminate controlled environments (e.g. isolators) is the preferred method due to several advantages to other decontamination procedures and decontaminating agents. Each H_2O_2 decontamination cycle ends with an aeration phase in order to reduce the H_2O_2 concentration to a specified limit. In addition to process-controlled parameters, e.g. rate of air-exchange, the aeration time is also influenced by the H_2O_2 absorption/desorption behavior of all exposed construction materials used in the controlled environment. The evaluation of the H_2O_2 absorption/desorption behavior of a material will be performed according to VDI 2083 Part 20.

6.1 Experimental design

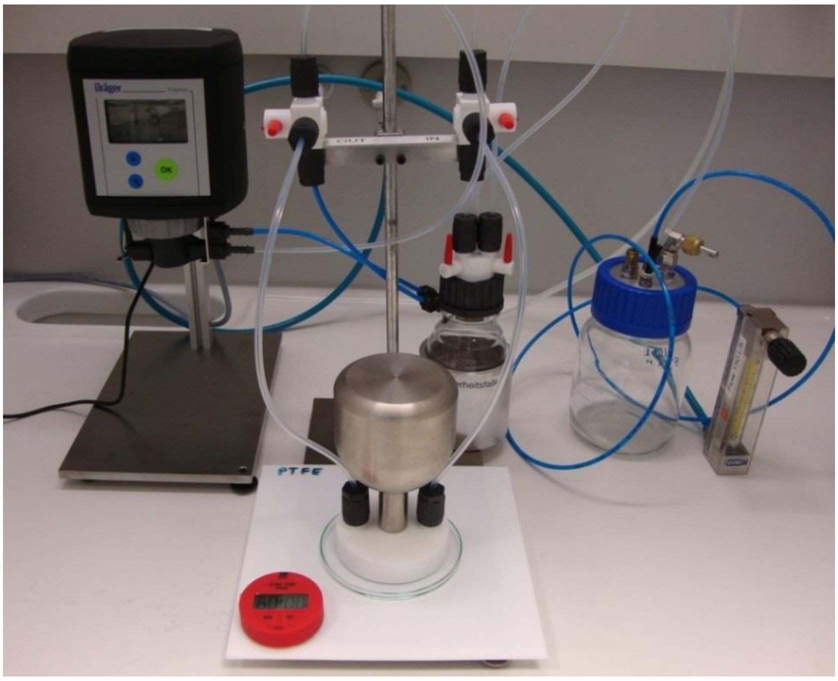


Figure 68 Experimental design. Left: H_2O_2 measurement device; center: exposure chamber, right: H_2O_2 source

A 1 L Schott laboratory glass bottle containing 200 ml of a 10 % hydrogen peroxide solution formes the H_2O_2 source. Ultra clean air is used as supply air with a volume flow of 150 l/h.

The following test parameters will be used according to VDI 2083 Part 20:

- Diameter: 65 mm
- Height: 5 mm
- Volume: 16.5 cm^3
- H_2O_2-exposed surface area: 33 cm^2
- H_2O_2 vapor concentration: 40 ± 20 ppm(V)
- Exposure duration: 60 min
- Purge flow rate: 150 l/h
- Measurement flow rate: 100 l/h
- Excess air flow rate: 50 l/h
- Air exchange rate (aeration): 100 min^{-1}

The exposure chamber is pressed onto the material sample supported by a weight. No hermetical seal encloses the gap between the exposure chamber and the sample allowing the excess air flow rate to escape. PFA tubing is used for all connections in contact with H_2O_2.

The H_2O_2 measurement device (Dräger Polytron 7000 with a corresponding low-concentration H_2O_2 sensor) is purged actively with 100 l/min during aeration.

6.2 Measurement strategy

The materials are exposed to H_2O_2 for 60 minutes. Subsequentely the chamber is flushed with ultra-pure air (aeration). Any H_2O_2 absorbed by the material desorbs from the material surface into the gas stream during the aeration step. The H_2O_2 concentration is measured online and illustrated in a graph with a logarithmic y-axis.

6.2.1 K-value

The k-value (in min) is the time required for the H_2O_2 concentration to reach 1/10 of the maximum concentration at the beginning of the aeration phase.

$$\mathbf{k = t\,(1/10\ c_{max}) - t\,(c_{max})}$$

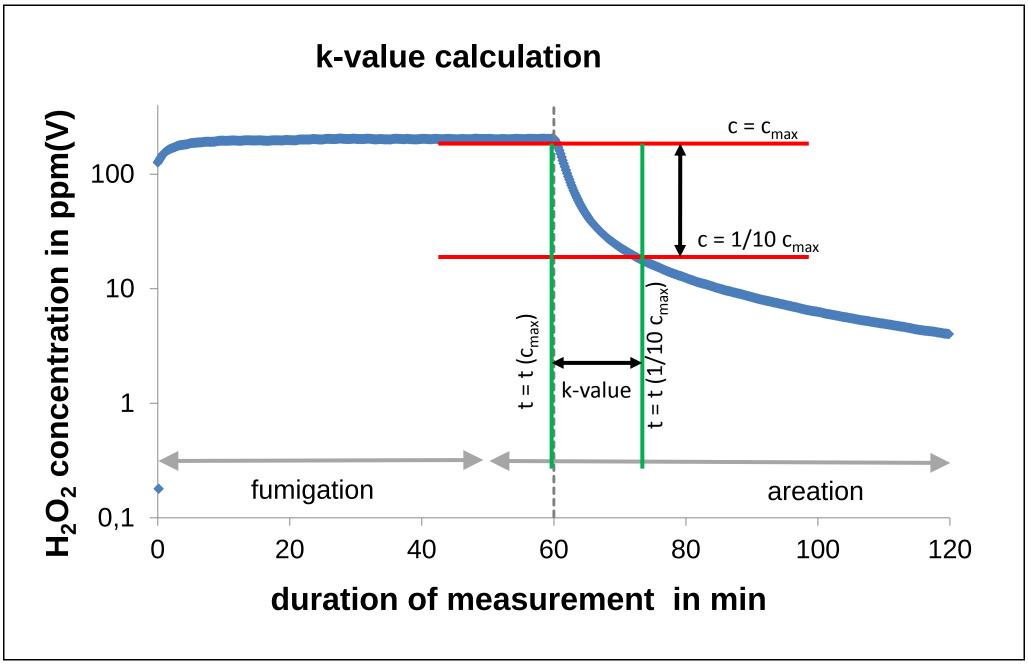


Figure 69 Calculation of the k-value

All samples are measured in triplicate in order to obtain three k-values and thus prove reproducibility. The average k-value of the blank measurement is subtracted from the individual k-values. The mean k-values correspond with the following classification:

K-value	H_2O_2 absorption and desorption kinetics: classification
≤ 5 min	non-absorptive
> 5 - ≤ 15 min	fast
> 15 - ≤ 60 min	medium
> 60 min	slow
Not determinable due to catalytic activity	catalytic

Figure 70 H_2O_2 absorption and desorption kinetics: classification

6.3 Results

6.3.1 Blank value

The blank value of the exposure chamber was measured three times:

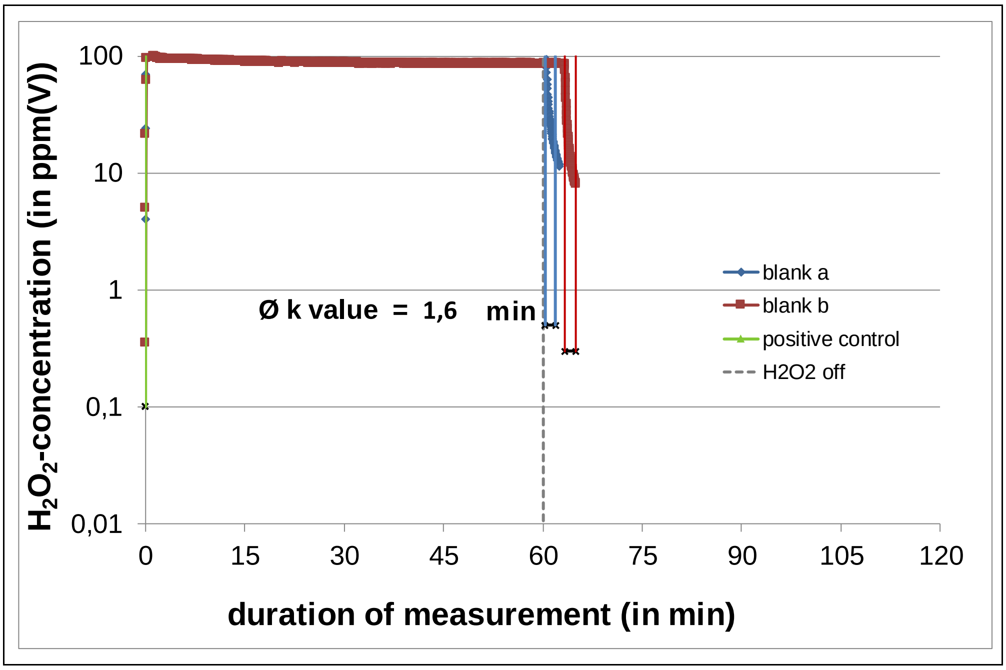


Figure 71 Blank value

6.3.2 Granite Standard Coil Coated Steel

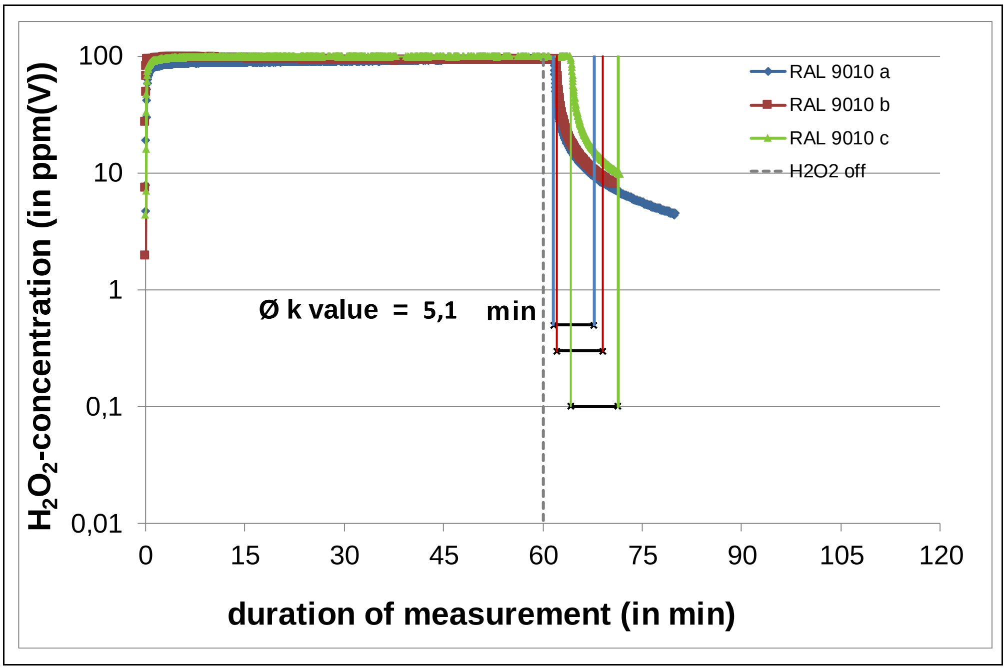


Figure 72 Absorption/Desorption: Granite Standard Coil Coated Steel

6.3.3 Formica High Pressure Laminate

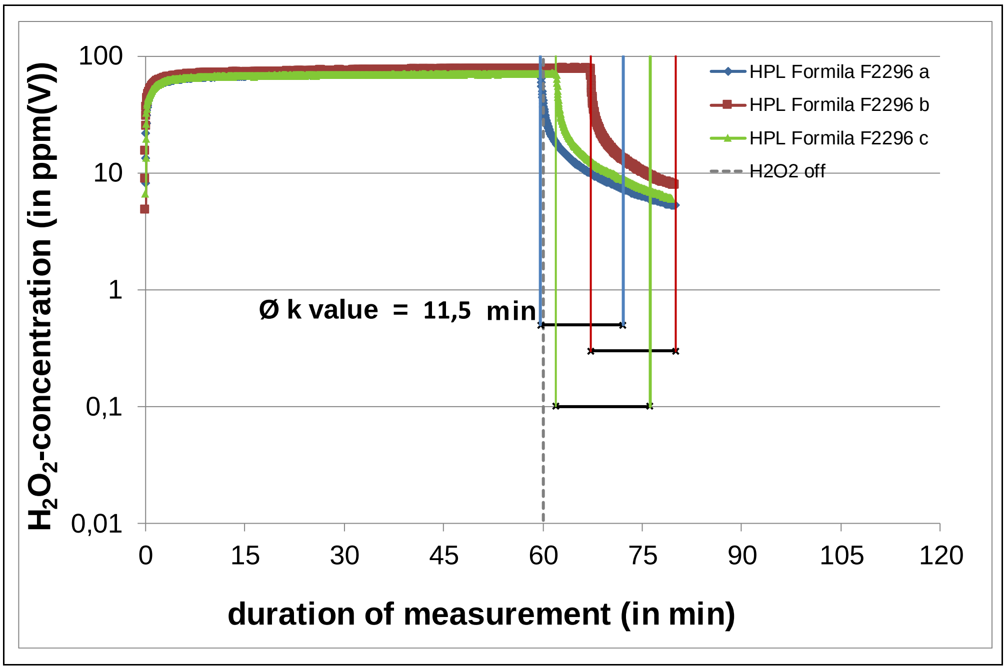


Figure 73 Absorption/Desorption: Formica High Pressure Laminate

6.4 k-values

For each measurement the materials were tested in triplicate. The following k-values, average k-values (Ø) and corresponding standard deviations (S.D.) were determined:

Test piece	Material	K-value [min]	Ø k-value [min]	S.D. [min]
TP00	Blank value	2.04	1.6 (blank value)	0.04
		2.08		
		2.00		
TP02	Granite Standard Coil Coated Steel	4.5	5.1 (fast)	0.5
		5.3		
		5.6		
TP03	Formica High Pressure Laminate	10.8	11.5 (fast)	0.9
		11.2		
		12.5		

Figure 74 k-values of tested materials – numerical values

7 Assessment of conformity with GMP regulations and EHEDG conception and design recommendations

7.1 Requirements

In order to assess an operating utility for use in clean manufacturing conditions with regard to conformity with relevant regulations and guidelines, expertises and metrological tests are carried out, such as those required to determine cleanroom suitability. The expertises evaluate the suitability of an operating utility for use in clean manufacturing areas, taking especially contamination behaviour and the constructional design of air-conducting areas with regard to particle deposition into consideration. Suitability regarding inspection, cleaning and disinfection is also assessed as a core requirement of the relevant regulations.

Analyses are carried out based on important norms and regulations relevant to the field of clean manufacturing.

- EHEDG (European Hygienic Engineering & Design Group)
- GMP (Good Manufacturing Practice)
- ISO (International Organization for Standardization)
- DIN (German Institute for Standardization)

The guidelines list conception and design specifications or give recommendations regarding the design, technical realization and construction of an operating utility. The conformity assessment is performed based on a visual evaluation of the test piece as well as on documentation and information supplied to the Fraunhofer IPA for qualification purposes.

The following criteria are assessed:

- Materials used
- Material pairings
- Geometries of materials implemented
- Joining techniques
- Constructional details
- Components used
- Manufacturing processes
- Surface coatings/coating systems

By assessing these criteria, the expertises are able to determine the suitability of the operating utility for use in GMP-conform manufacturing environments, focusing especially on contamination avoidance and on the ability to clean and disinfect the operating utility.

7.1.1 Generation and cause of contamination

Material and surface characteristics and also the constructional design of components are often a cause of contamination.

Risks arise as a result of:

- The electrostatic properties of the surfaces of operating utilities.
  Electrostatic effects, stimulated for example by wipe-cleaning, may cause surface contamination to accumulate. Induced or spontaneous detachment may cause high or critical concentrations of contaminants.

- Materials which are not resistant to chemicals.
  The use of aggressive cleaning and disinfecting agents may attack or destroy the surfaces of unsuitable operating utilities and cause increased surface roughness. This makes it difficult or impossible to clean and disinfect surfaces adequately.
- Sharp edges, rough joins or protruding screw heads make it difficult to clean and disinfect an operating utility.
- Constructional details may facilitate the deposition and accumulation of contamination, e.g. dead zones, depressions.
- Materials used may serve as a food source for microorganisms, enabling them to accumulate and multiply.

7.1.2 Removing contamination

Material and surface characteristics and also the constructional design of various components play a decisive role in the effective removal of contamination.

- After their assembly, it must still be possible to inspect, clean and disinfect all component surfaces efficiently using a reasonable amount of effort. Alternatively, an easy dismantling of the components is necessary.
- Workmanship of joins and mounted fixing elements (seams, corners, cavities, etc.) may not impair the ability to clean and disinfect the utility.
- The surface roughness of the components may not facilitate the accumulation of contamination.

7.1.3 Materials and surfaces

In manufacturing environments conforming to GMP regulations, the avoidance of microbial and particulate contamination of the end-product is a core issue. The selection of appropriate materials has a major influence on the suitability of operating utilities in clean manufacturing areas.

The ability to effectively clean and disinfect an operating utility is mainly dependent upon its surface structure. If cleaning is impaired because a surface is too rough or the surface coating has been damaged, microbial risks cannot be reduced to an acceptable level. In order for a surface to be optimally cleanable, EHEDG Document 8 "Hygienic equipment design criteria" and EHEDG Document 10 "Hygienic design of closed equipment for the processing of liquid food" recommended, that care should be taken to ensure that the surface is smooth and non-porous. The surface roughness of parts coming into contact with products must be $R_a < 0.8$ µm.

7.1.4 Design and geometry

The geometric design of operating utilities or single components significantly affects their suitability for use in clean manufacturing environments. If, for example, there are counter drafts and “dead water zones” in an air flow, there is a risk that particles generated during operation of the system will not be extracted by the first airflow of the cleanroom. This may result in particles or microorganisms accumulating in indentations or crevices. Contamination which has accumulated in this way cannot be removed through cleaning. Microorganisms coming into contact with low concentrations of disinfectants may then develop a resistance to them. Such germs, which mutate to become disinfection-resistant, are then “cultivated” as a result.

“Equipment which is difficult to clean will need procedures which are more serve, require more aggressive chemicals and longer cleaning and decontamination cycles. Result will be higher costs, reduce availability for production, reduce lifetime of the Equipment, and more effluent.”

“Consequently dead legs, gaps and crevice where microorganisms can harbor and multiply must be avoided.” (EHEDG Document 8)

Such counterdrafts or inaccessible areas may form if, for example, unsuitable screw heads have been selected for joining materials with screw connections, or because the workmanship of weld seams is poor. If processes are carried out without due care and attention, the hygienic strategies developed in the design phase of an operating utility may be impaired.

7.2 Assessment of the test piece

The assessment is based on the suitability of the complete test piece - consisting of wall and ceiling elements, a door and window elements - for use in cleanrooms and its ability to be cleaned effectively. Both the interior and exterior have been assessed, assuming that the interior will be the area with the higher cleanroom class.

Figure 75 Wall and ceiling system

7.3 Materials implemented

The materials used in the TP01 may not impair the ability to clean or disinfect it. Therefore, care is to be taken to ensure that the surfaces of these materials are not porous but instead smooth and easy to clean. They must be resistant to the cleaning and disinfection agents utilized.

The following materials were utilized:

Component	Material
Ceiling panel	Pre-painted steel
Wall panel I	Formica High Pressure Laminate (HPL)
Wall panel II	Granite Standard Coil Coated Steel
Door frame	Aluminum
Door	Granite Standard Coil Coated Steel
Windows	Safety glass
Joint seal	SIKA Pro 3 Silicone
Door sealing lip	TPE
Corner profile / Floor profile	Aluminum
Round corner profile	PVC

All materials utilized largely fulfill GMP requirements for cleanroom-suitable manufacturing.

7.4 Assessment of details TP01

7.4.1 Wall and ceiling panels

Assessment:

The glossy wall and ceiling panels are smooth, free of cracks and impermeable, indicating a very low surface roughness. The entire surface is easy to clean and disinfect and meets the requirements of hygienic production.

Potential for optimization:

The design of the wall and ceiling panels meets the requirements of the GMP Guideline Annex 1, as well as the specifications of EHEDG, Document 13 "*Hygienic design of equipment for open processing*".

Figure 76 Wall and ceiling panels

7.4.2 Material joints

Assessment:

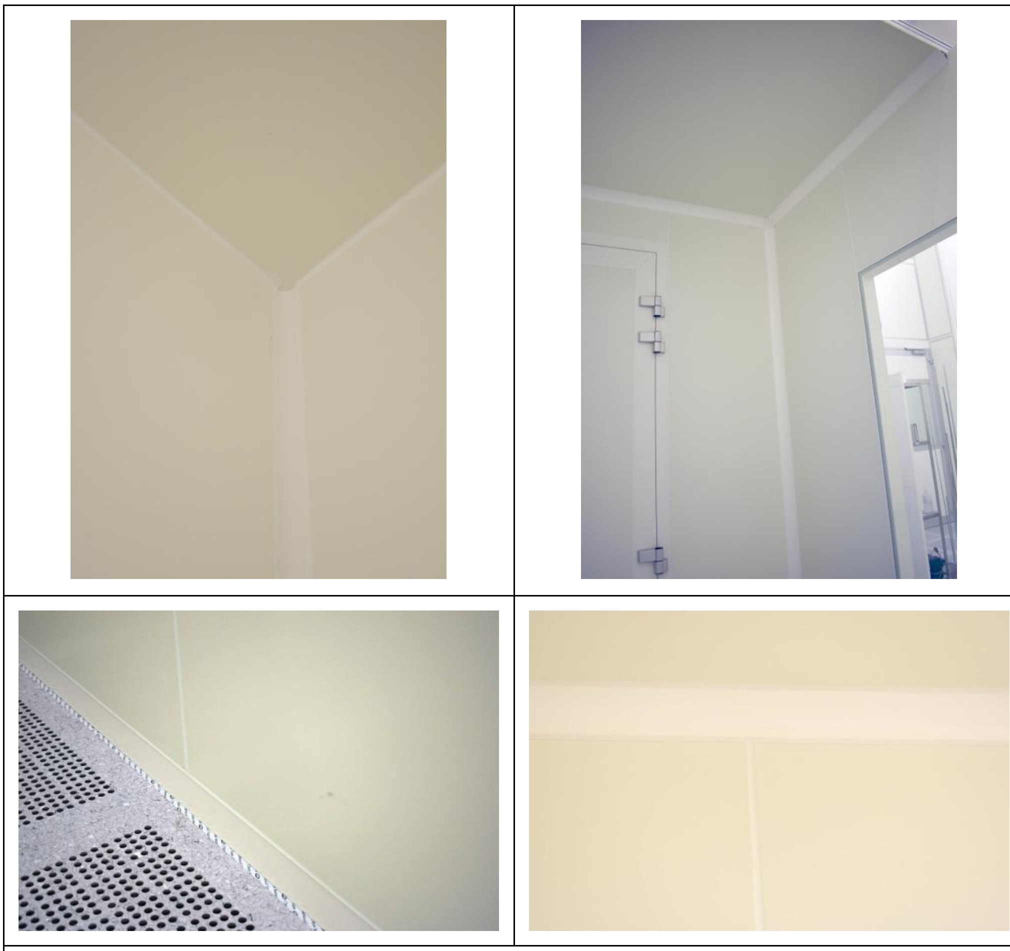
The wall, ceiling and glass elements are joined with silicon.
The joints between the different materials are continuous and flat. The corners and transition areas between the walls and the ceiling have been designed with silicon joints or inner corner panels, making them easy to clean.

Potential for optimization:

The material joints comply with the requirements of the GMP Guideline Annex 1, as well as the requirements of the EHEDG, Document 44 "*Hygienic design principles for food factories*".
There is no potential for optimization here.

Figure 77 Material joints

7.4.3 Connecting profiles



Assessment:

The connecting profiles (floor connection profiles, ceiling connection profiles, corner profiles) are made of PVC or coated aluminum. The profiles are smooth and shiny. The corner profiles are rounded and have a large radius of curvature to ensure good cleanability.

Potential for optimization:

The geometric design of the connection profiles meets cleaning and disinfection requirements, as well as the specifications of EHEDG, Document 13, "*Hygienic design of equipment for open processing*". There is no potential for optimization here.

Figure 78 Connecting profiles

7.4.4 Floor connection profile

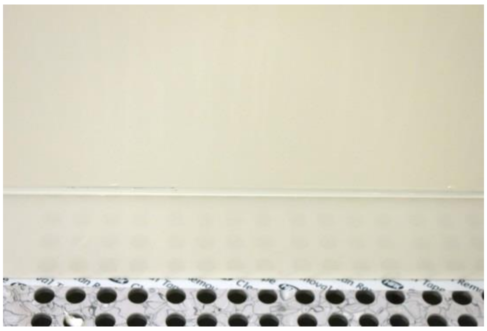
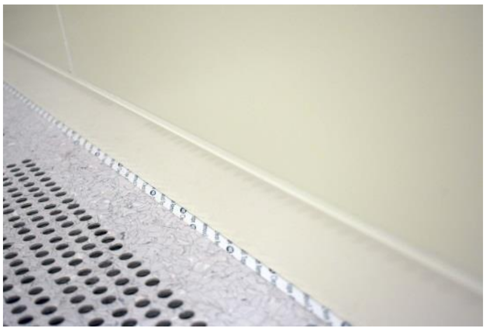
	
Assessment: The flooring is joined to the wall elements via a floor connection profile and a silicon joint. The floor connection profile is flush with the wall elements. However, this creates a right angle at the transition to the floor. The silicon joint has been applied continuously, smoothly and carefully.	
Potential for optimization: The ability to clean and disinfect this area effectively is slightly impaired here due to the right-angled transition to the floor. A transition with a chamfer is preferable. DIN EN 1672-2 "Food processing machinery - Basic concepts - Part 2: Hygiene requirements" and the EHEDG, Document 44 "*Hygienic design principles for food factories*" provides more detailed information on the design of inner corners and angles.	

Figure 79 Floor connection profile

7.4.5 Transition between corner profile and floor connection profile

Assessment:

At the transition of the rounded corner profile to the floor profile, there is an opening which cannot be completely closed by the joint material.
Here microorganisms or other contaminants can accumulate and lead to spontaneous contamination.

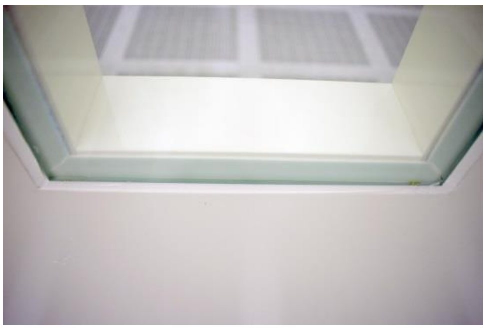
Potential for optimization:

To prevent liquids or particles from entering gaps and cracks, joints and material transitions should be sealed and fully hygienic. Consistent cleanability is only ensured by avoiding undercuts, gaps or cracks, protruding edges and dead spaces, as described in DIN EN 1672-2 "*Food processing machinery - Basic concepts - Part 2: Hygiene requirements*".

To ensure a clean and seamless transition, the profiles must be perfectly aligned with one other.

Figure 80 Transition between corner profile and floor connection profile

7.4.6 Transition between glass elements and wall / door



Assessment:

All glass elements have been mounted in such a way that a flat surface is created in the product area. The joints are continuous and have been applied with care. This ensures good cleanability.

Potential for optimization:

There is no potential for optimization here.
The detail considered meets the requirements of GMP Annex 1, "Surfaces in clean areas should be smooth and impermeable, free of cracks and damage".

Figure 81 Transition between glass elements and wall / door

7.4.7 Air duct

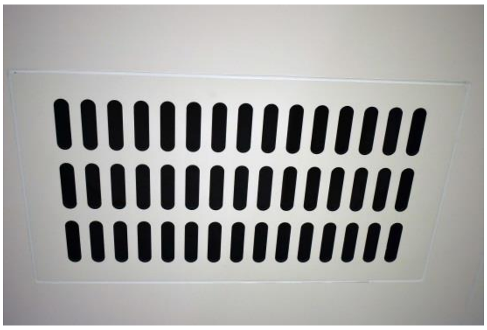
<table>
<tr><td></td><td></td></tr>
<tr><td colspan="2">Assessment:
The air duct is integrated into a wall panel near the floor and mounted into the wall panel with silicon joints. The air openings are rounded and large enough to ensure cleanability in this area.</td></tr>
<tr><td colspan="2">Potential for optimization:
The geometric design of the air duct meets cleaning and disinfection requirements, as well as the specifications of the EHEDG, Document 13, "Hygienic design of equipment for open processing". There is no potential for optimization here.</td></tr>
</table>

Figure 82 Air duct

7.4.8 Door

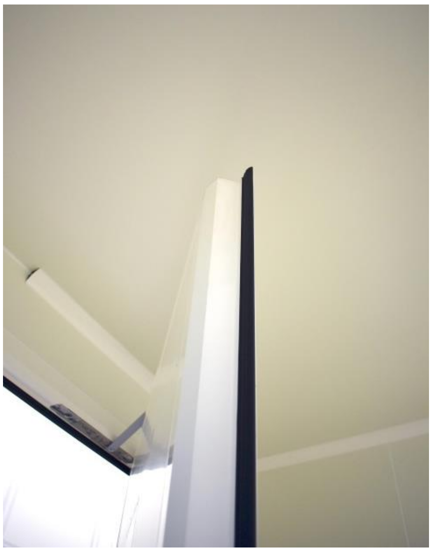
	
	
Assessment: The self-closing door is fitted with a glass element and has a seal all the way around. The door has been mounted flush with the wall system. There are no undercuts or recesses.	
Potential for optimization: The geometric design of the door meets cleaning and disinfection requirements, as well as the specifications of EHEDG, Document 44, "*Hygienic design principles for food factories*". There is no potential for optimization here.	

Figure 83 Door

7.4.9 Door handle

Assessment:

The door handle has no horizontal surfaces, liquids can drain unhindered to the floor. It is attached to the door with a small hexagon-head socket screw. This screw has a recess into which dirt can penetrate. This makes this area difficult to clean and disinfect. There is a seal at the transition between the handle and cover.

Potential for optimization:

The geometric design of the door handle meets cleaning and disinfection requirements, as well as the specifications of the EHEDG, Document 13, "*Hygienic design of equipment for open processing*".
The screw connection with a hexagon-head socket screw should not be used. Alternatively, the screw head should be sealed.

Figure 84 Door handle

7.4.10 Door hinges

Assessment:

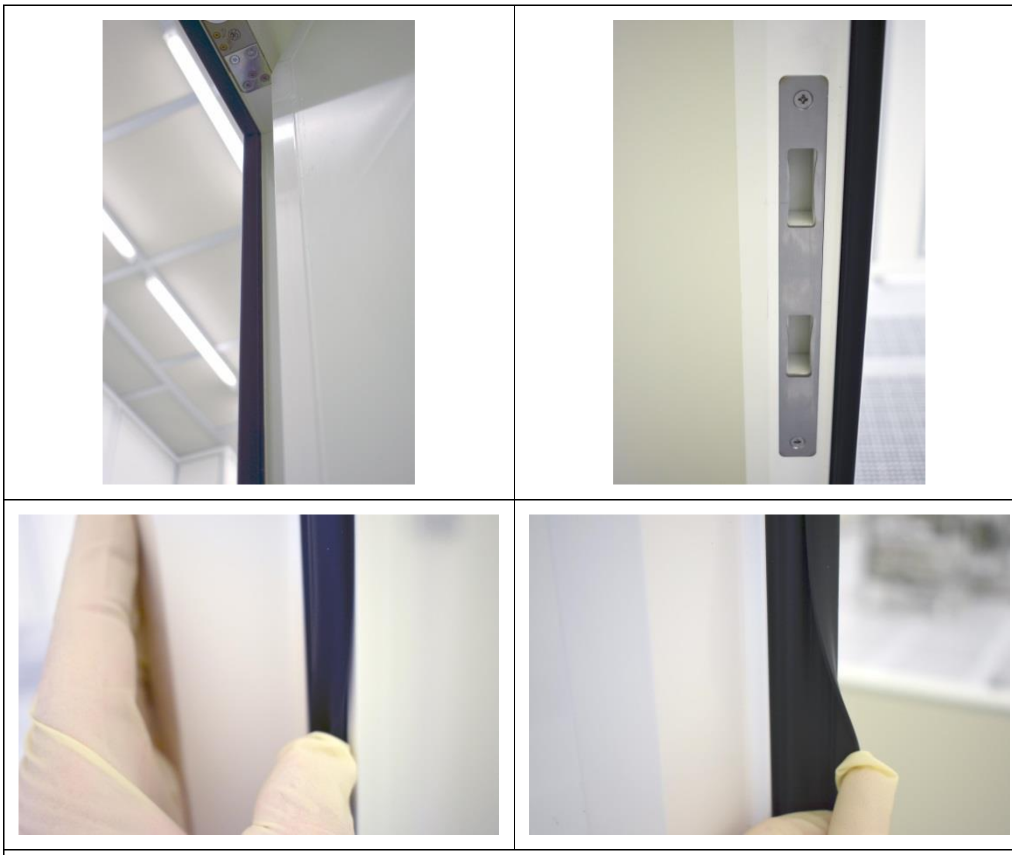
The door hinges are covered to prevent the entry of liquids and dirt. The geometric design facilitates cleaning through good accessibility. However, there are minimal horizontal surfaces. The black cap is embossed. Embossing can slightly impair the cleanability of this area.

Potential for optimization:

The geometric design of the door hinges meets cleaning and disinfection requirements, as well as the specifications of the EHEDG, Document 13, "*Hygienic design of equipment for open processing*".
Embossing should generally be avoided.

Figure 85 Door hinges

7.4.11 Door seal



Assessment:

The all-round door seal is fixed to the door frame by adhesive. However, the adhesive has not been applied continuously, thus allowing dirt to accumulate behind the door seal. This area cannot be cleaned and disinfected effectively.

Potential for optimization:

The use of a removable seal is preferable to a bonded seal because it can be removed for cleaning and cleaned separately. This is the only way to prevent contamination from accumulating and being spontaneously released into the production area. If adhesive cannot be avoided for the door seal, it must be applied in such a way so as to prevent dirt from getting behind the door seal and accumulating.

DIN EN 1672-2:2005: "*Food processing machinery - Basic concepts - Part 2: Hygiene requirements*", describes the required properties of such seals.

Figure 86 Door seal

7.4.12 Interlock control panel

Assessment:

The interlock control panel has been mounted flush with the cleanroom wall. The button has beveled edges and the lights are flat with no horizontal surfaces, enabling liquids to run off unhindered.
The panel has been mounted with cross-head screws. Here cleanability is slightly impaired due to the undercuts caused by the screws.

Potential for optimization:

The material and design of the interlock control panel correspond to the specifications. There is no potential for optimization here.
If screw connections cannot be avoided, the number of screws utilized should be kept to a minimum.
If cross-head or hexagon-head socket screws are used, they should be fitted with a cover. However, the use of hygienic screws is preferable. The EHEDG guideline describes recommended types of screws. EHEDG Document 13 "Hygienic design of equipment for open processing".

Figure 87 Interlock control panel

7.5 GMP and hygiene assessment

7.5.1 General information

The current guideline for good manufacturing practice issued by the European Commission (GMP guideline) lists statutory requirements for manufacturing sterile drugs and other products under hygienic conditions.

Annex 1 of the GMP guideline contains more detailed information regarding requirements of hygienic manufacturing environments. Clean areas for manufacturing sterile products are classified according to the environmental characteristics required. Each manufacturing process demands a certain degree of environmental cleanliness in an operating state in order to minimize the risk of contaminating relevant products or materials with particles or microorganisms. To fulfill operative conditions, areas must be constructed in such a way so as to ensure that specific degrees of air cleanliness prevail when in a resting state. The resting state is the state when the complete technical equipment is installed and ready for operation without the presence of any staff. The operating state is the state when the equipment is operated in the intended manner by a specified number of staff.

7.5.2 GMP cleanliness classes

Four different cleanliness classes apply in the manufacture of sterile drugs:

- **Cleanliness Class A: sterile areas**
  Localized zones for carrying out high-risk work procedures, e.g. filling procedures, areas containing stopper receptacles, open ampoules and phials, making up aseptic compounds. Such conditions are safeguarded through the use of laminar airflow systems with a flow rate of 0.45 m/s + 20 %.
- **Cleanliness Class B: sterile areas**
  For aseptic preparations and filling; these environments must encircle Cleanliness Class A zones.
- **Cleanliness Classes C and D: clean areas**
  Laboratories and manufacturing areas for less critical processes required in the manufacture of sterile products.
- **GMP Cleanliness Classes E and F: areas without a defined particle count or level of biocontamination**
  These may be manufacturing areas, laboratories, documentation areas, offices, break rooms and other areas.

The following table gives a classification of cleanliness levels according to the number of particles contained in the air:

Cleanliness Class	Maximum permissible particle count per m³ in a resting state		Maximum permissible particle count per m³ in an operating state	
	> 0.5 µm	> 5 µm	> 0.5 µm	> 5 µm
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 fixed	not fixed

Figure 88 Classification of air quality in the manufacture of sterile products: Particles (GMP Annex 1)

In an unmanned environment, the particle counts shown in the column marked "resting state" should be achieved on completion of the work processes after a short "clean up" phase of 15-20 minutes (guideline). The particle counts shown in the table for Cleanliness Class A in an operating state are to be upheld in the zone directly adjacent to the product if products or open containers are exposed to the environment.

The following table gives a classification of cleanliness levels according to the number of microorganisms detected:

Cleanliness Class	Recommended limiting values for microbiological contamination		
	Air sample [CFU/m³]	Sedimentation plates (Ø 90 mm) [CFU/4 hours]	Contact plates (Ø 55 mm) [CFU/plate]
A	< 1	< 1	< 1
B	10	5	5
C	100	50	25
D	200	100	50

Figure 89 Classification of air quality in the manufacture of sterile products: Biocontamination (GMP Annex 1)

Fraunhofer IPA

The following table gives examples of work processes carried out in the various cleanliness classes.

Cleanliness Class	Examples: work processes for aseptic preparations
A	Aseptic preparation and filling processes
B	Ambient area for GMP A premises (if no isolator technology is used)
C	Preparation of solutions requiring filtration
D	Handling constituents after washing

Figure 90 Examples of work processes in various cleanliness classes

7.5.3 Suitability of operating utilities for use in the various GMP cleanliness classes

The GMP guideline states that none of the equipment used in manufacturing processes may represent a risk to the product. No piece of equipment coming into contact with the product may interact with it as this would impair product quality and represent a further risk. In clean areas, all exposed surfaces must be smooth, impermeable and free of fissures, both to minimize particle and microorganism counts and also to permit the repeated use of cleaning and disinfection agents. The GMP guideline states that manufacturing equipment must be in good condition, be completely cleanable and not represent a source of contamination to the product.

By assessing particulate emission from of an operating utility and the microbiological cleanliness of its surfaces, direct information can be obtained regarding suitability for use in a specific GMP cleanliness class.

If an operating utility has been assessed with regard to its conception and design as laid down in the guidelines of EHEDG, DIN EN 1672-2, ASME BPE (2007), NSF/ANSI/3A 14159-1 (2000) and other relevant norms, a general suitability of the operating utility for use in the hygienically critical manufacturing areas of Cleanliness Class A/B in accordance with GMP may be awarded if these norms have been completely observed. However, this only applies to the operating utility in a resting state. Once it has been installed into a complete production plant, the overall production environment must be assessed. If there is a possibility that particles could be emitted from the utility when in operation, this must be recorded and assessed separately because the relevant GMP cleanroom classes state concrete limiting values for such cases. The final position of the operating utility in the production plant also plays a decisive role with regard to the GMP cleanliness class in which it may be implemented. A final determination of the suitability of an operating utility for use in a defined GMP cleanliness class can therefore only be made on site.

7.6 Summary

It is not always possible to conform to all the recommendations contained in guidelines concerned with cleaning and disinfection without impairing functionality. However, it is important that critical areas are designed as carefully as possible in accordance with the relevant guidelines. In the **Brecon Cassette Panel System** from **Brecon Cleanroom Systems B.V.**, most of the design principles were taken into account. There is potential to optimize the few critical areas that were identified.
The overall design of the cassette panel system complies with recommendations on clean and hygienic manufacturing.

Due to the aforementioned design features of the modular wall and ceiling system **Brecon Cassette Panel System from Brecon Cleanroom Systems B.V.** that was investigated by Fraunhofer IPA, and under consideration of the optimization potential listed, the system is declared **suitable for use in clean and hygienic manufacturing areas**.

The assessment is based on the almost total ability to clean and disinfect the wall and ceiling system and – with only a few exceptions – the fulfillment of conception and design recommendations made by EHEDG, ISO 14159 and 1672-2.

In principle, the system is declared suitable for use in hygienic areas fulfilling max. **GMP Cleanliness Class A**. However, this only applies to the tested operating utility in a resting state. An overall reassessment would need to be made after installation in a manufacturing environment.