complean Engineering

Kurzvortrag im Rahmen des
SCC Events am 05. Juli 2021

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YY0033
Good manufacturing practice for medical devices

Facts & Figures

Rahmendaten

- Gegründet 2016
- Firmensitz in Affoltern am Albis
- 7 Mitarbeiter
  - *angestrebt 8-12 MA*
- Umsatz 2020 ~ 1Mio CHF

Warum complean?

- Mehr als 25 Jahre Erfahrung ….
  - … als Kunde
  - … als Betreiber
  - … als Planer
  - … im regulierten Umfeld
- Innovative Lösungskonzepte
- Hoher Grad der Vernetzung

Kompetenzfelder

- Reinraumtechnik
- Pharmatechnik
- Verfahrenstechnik
- Lebensmitteltechnologie
- Mikrobiologie
- Qualifizierung & Validierung
- Projektmanagement
- Prozessmanagement

Leistungskatalog

Design & Engineering

Funktionelle Planung
- Infrastrukturelle Konzepte
- Technische Systeme

Konzepte
- Conceptual Design
- Basic Design
- Detail Design

Dokumentation
- User Requirements
- Lastenhefte

Risikomanagement
- Technische Risikoanalyse
- Prozess-Risikoanalyse

Prozessdesign
- Technische Prozesse
- Herstellprozesse
- Supportprozesse

Realisation & Project Management

Projektmanagement
- Überwachen & Steuern von Terminen, Qualität und Kosten

Lieferantenmanagement
- Betreuen der Lieferanten
- Koordinieren der Schnittstellen zwischen Kunde und Lieferant

Realisierung
- Begleiten der Realisierungsphase
- Änderungsmanagement
- Abweichungsmanagement

Startup & Commissioning

Startup & Inbetriebnahme
- Durchführen und Begleiten der Inbetriebnahme-aktivitäten
- Koordinieren des «Troubleshootings» während der Inbetriebnahme

Qualification & Validation

Equipment Qualifizierung
- Planen der Qualifizierung
- Durchführen der Qualifizierungstests
- Dokumentation

Prozessvalidierung
- Planen der Validierung
- Begleiten der Validierungsaktivitäten
- Dokumentation

Handover
- Begleiten der Übergabe an den Betreiber
- Begleiten der Übergabe an den Nutzer

Visualisierung, Virtualisierung

Prozessoptimierung, KVP

Qualitätsprozesse (z.B. Deviation Management) & Change Management

Measurement & Services

Messungen
- Reinraumspezifische Messungen
- Physikalische Parameter
- Periodische Messungen oder Einzelmessungen

Audits
- Lieferantenaudits
- Interne Audits
- Kundenaudits
- Vorbereiten von Audits
- Begleiten von Audits

Coaching
- Projektspezifisches Coaching

Moderation
- Projektspezifische Workshops

Trainings & Seminare
- Audits - professionelle Vorbereitung und Durchführung
- Qualifizierung & Validierung im GMP-pflichtigen Umfeld

Happy customers ….

C 30

Record No. 0854-2001

Medical Industry Standard

of the People's Republic of China

YY 0033-2000

Replacing YY/T 0033-1990

Good manufacture practice for sterile medical devices

无菌医疗器具生产管理规范

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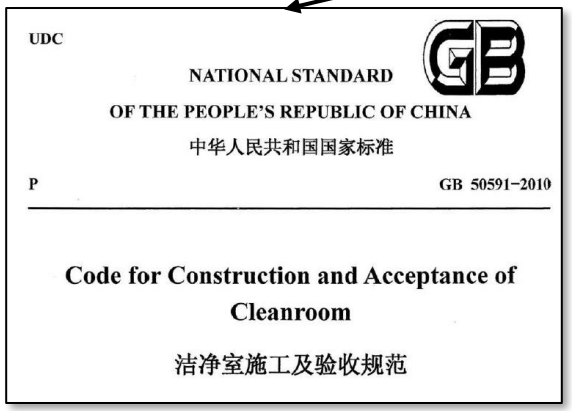

UDC

NATIONAL STANDARD

OF THE PEOPLE'S REPUBLIC OF CHINA

中华人民共和国国家标准

P GB 50591-2010

Code for Construction and Acceptance of Cleanroom

洁净室施工及验收规范


GB

NATIONAL STANDARD OF THE

PEOPLE'S REPUBLIC OF CHINA

ICS 13.040.30

C 30

GB/T 16292-2010

Replacing GB/T 16292-1996

Test method for airborne particles in cleanroom (zone) of the pharmaceutical industry

医药工业洁净室(区)悬浮粒子的测试方法


GB

NATIONAL STANDARD OF THE

PEOPLE'S REPUBLIC OF CHINA

ICS 13.040.30

C 30

GB/T 16294-2010

Replacing GB/T 16294-1996

Test method for settling microbe in clean room (zone) of the pharmaceutical industry

医药工业洁净室（区）沉降菌的测试方法


GB

NATIONAL STANDARD OF THE

PEOPLE'S REPUBLIC OF CHINA

ICS 13.040.30

C 30

GB/T 16293-2010

Replacing GB/T 16293-1996

Test method for airborne microbe in cleanroom (zone) of the pharmaceutical industry

医药工业洁净室(区)浮游菌的测试方法

(VDI 2083)

(ISO 14644-3)

(DIN/EN 17141 oder Annex 1)

YY0033 - Inhalt

Kapitel 5 – production environment

5.1.1 Location of factory shall be chosen at areas with good sanitary condition, fresh air, low concentration of dust and microbe in air, good natural environment and free from hazardous gas.

5.1.2 Location shall be far from the railway, port, airport, traffic artery, and factory, silo, stockyard that emit a lot of dust and hazardous gas and where have serious air pollution, water pollution, vibration or noise interference. Clean room shall not be less than 50m from municipal transport corridors.

5.1.5 "Four Nons" shall be met around production facility (non-ponding, non-weeds, non-garbage, non-generation of mosquito or fly). And it is better not to have naked land.

5.3.5 There shall be 1 water tap for up to 10 persons per shift. The water tap shall be non-manual system.

YY0033 – Annex A

Annex A

(Normative)

Cleanliness Classes for Clean Room (Area) of Sterile Medical Devices

Table A1

Cleanliness class	Maximum number of particles, piece/m³		Maximum permitted quantity of microorganism	
	≥0.5μm	≥5μm	Settling microbe, piece/dish	Airborne microbe, piece/m³
100-class	3500	0	1	5
10000-class	350000	2000	3	100
100000-class	3500000	20000	10	500
300000-class	10500000	≤60000	15	—

PIC GMP Annex 1 (2021 Draft)

Grade	Maximum limits for particulates ≥ 0.5 μm/m³		Maximum limits for particulates ≥ 5 μm/m³	
	at rest	in operation	at rest	in operation
A	3 520	3 520	Not applicable	Not applicable
B	3 520	352 000	Not applicable	2 900
C	352 000	3 520 000	2 900	29 000
D	3 520 000	Not defined[a]	29 000	Not defined[a]

Grade	Air sample cfu/m³	Settle plates (diameter 90 mm) cfu/4 hours [a]	Contact plates (diameter 55 mm) cfu/plate
A[b]	No growth[b]		
B	10	5	5
C	100	50	25
D	200	100	50

YY0033 – Annex B&C

B3 For implants, sterile medical device or unit package released accessories that are directly or indirectly contacted with circulated blood or bone hollow, production process of the parts and components (not cleaned) such as machining, final cleaning, assembling, primary packaging, and sealing shall be conducted at areas not less than 100000-class cleanliness level. Sterile medical device, which is implanted into blood and whose realization process such as production, assemble and package are realized in a local environment, shall be manufactured in the clean room (area) not less than 10000-class cleanliness (100-class is preferred).

B6 Implantable sterile medical device (including materials) adopting sterile operation technology shall be manufactured in local 100-class of 10 000-class clean room (area).

B7 The air cleanliness of area of cleaning, drying of clean work clothes, room of wearing clean work clothes, area of final cleaning and sterilization of special work accessories shall be one level below production area. Clean up and storage of sterile work clothes shall be at the clean room (area) of 10000-class.

Annex C

(Normative)
Environment Requirements and Monitoring for Clean Room (Area) of Sterile Medical Device

Table C1

Monitoring item		Technical index				Monitoring method	Monitoring frequency
		100-class	10000-class	100000-class	300000-class		
Temperature, °C		(when there is no special requirement) 18~28					1/shift
Relative humidity, %		45~65					1/shift
Wind speed, m/s		Horizontal laminar flow ≥0.4 Vertical laminar flow ≥0.3	—	—	—	JGJ 71-1990	1/month
Ventilation rate, time/h		—	≥20	≥15	≥12		1/month
Static pressure difference, Pa		Between clean room (area) of different cleanliness and non-clean room (area) ≥5					1/month
		Clean room (area) and outside ≥10					
Number of particles, piece/m^3	≥0.5μm	≤3500	≤350000	≤3500000	≤10500000	GB/T 16292-1996	1/quarter
	≥5μm	0	≤2000	≤20000	≤60000		
Number of airborne microbe, piece/m^3		≤5	100	500	—	GB/T 16293-1996	1/quarter
Number of settling microbe, piece/m^3		≤1	≤3	≤10	≤15	GB/T 16294-1996	1/week

YY0033 – Annex D & E

Annex D

(Informative)

General Procedure of Personnel In-and-Out of Clean Production Area

General procedure of personnel in-and-out of clean production area and sterile-operation clean production area are shown in Figure D1 and Figure D2.

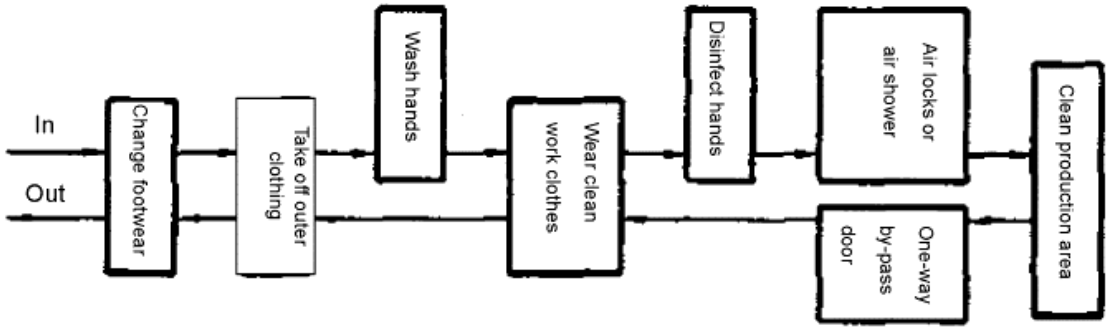


Figure D1 Procedure of Personnel In-and-Out of Clean Production Area

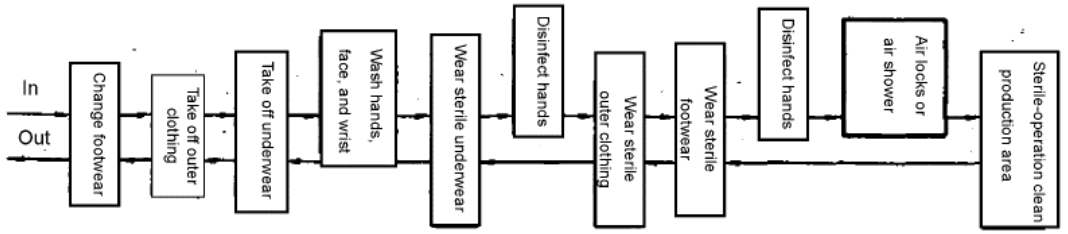


Figure D2 Procedure of Personnel In-and-Out of Sterile-Operation Clean Production Area

YY0033 – Code for construction

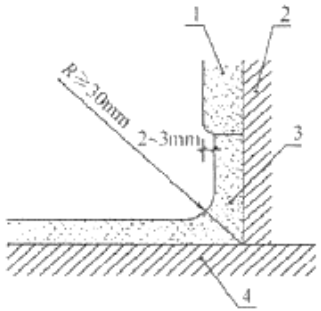


Figure 4.5.1 The Circular Arc of Integral Wall Corner

1—Wall; 2—Base course of wall; 3—Integral wall corner; 4—Ground

Table 5.2.13-1 The Maximum Air Leakage Rate for Unit Developed Area of Rectangular Snap-in Metal Duct

[$m^3/(h \cdot m^2)$]

Duct segment and accessories	Test pressure (Pa)	Maximum air leakage rate [$m^3/(h \cdot m^2)$]
Header duct (The duct segment connecting outlet and inlet of fan)	1500 or operating pressure P	$0.0117\times1500^{0.65}=1.36$ $0.0117\times P^{0.65}$
Main duct (The duct segment connecting header duct and branch duct or branch main duct)	1000 or operating pressure P	$0.0352\times1000^{0.65}=3.14$ $0.0352\times P^{0.65}$
Branch duct (the duct segment connecting air outlet, including adaptor spool)or branch main duct	700 or operating pressure P	$0.0352\times700^{0.65}=2.49$ $0.0352\times P^{0.65}$

Note: The air leakage rate of round metal snap-in and flange connection duct as well as non-snap-in and non-flange connection duct shall be calculated according to 50% of the value given in the following Table.

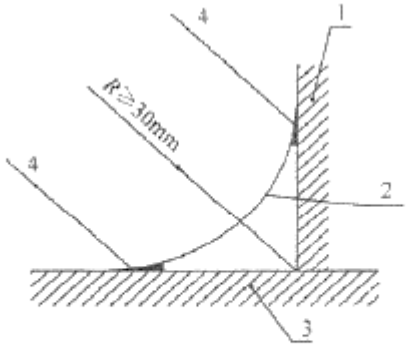
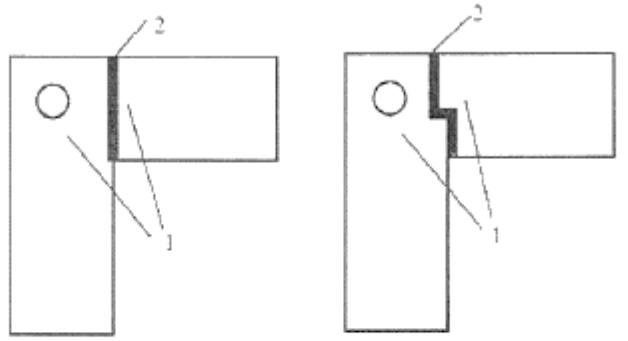


Figure 4.5.2 The Circular Arc for Transitional Wall Corner of Section Bar

1—Wall; 2—Wall corner of section bar; 3—Ground; 4—Sealing build-in material



(a) Abutting joint: incorrect (b) Echelon joint: correct

Figure 5.3.3 Joints of Flange Sealing Gasket

1—Sealing gasket; 2—Sealant

Zusammenfassung

- Aktuell gültiges Regelwerk, wenn auch aus dem Jahr 2000
- Geltungsbereich: Sterile Medizinprodukte
- Noch weitgehend unbekannt & unbeachtet in Europa
- Nur eine (1) englische Übersetzung verfügbar, an einzelnen Stellen unklar / fragwürdig
- Unterschied zu den «gewohnten» Normen in Europa / USA
  - Teilweise klare Angaben was wann zu tun ist
  - Teilweise signifikant andere Spezifikationen für vergleichbare Anforderungen

Abschluss - Fragen

Vielen Dank für Ihre Aufmerksamkeit!