Table I. Summary Table for Temperature, Humidity, Air Change and Pressure Differential Requirements

NOTE: The information in this guide is presented as a guide for design of cleanrooms; it is not intended to supersede existing site procedures or validation tests used to determine existing cleanroom standards.

Consult Design Engineering Firm for proper LotterBhanson - C.E.C.H.S. Room Classification based on operations covered in ISPE Baseline Guides.[8,9,10]

LotterBhanson - C.E.C.H.S. Designation	ISO 5 / Grade A	ISO 7 / Grade B	ISO 8 / Grade C	Grade D	CNC Level 2/3	CNC Level 1
Other Industry Designations	Grade A [Ref 2] ISO 4.8 in operation [Ref 2] ISO 4.8 at rest [Ref 2] Class 100 [Ref 4]	Grade B [Ref 2] ISO 7 in operation [Ref 2] ISO 5 at rest [Ref 2] Class 10,000 [Ref 4]	Grade C [Ref 2] ISO 8 in operation [Ref 2] ISO 7 at rest [Ref 2] Class 100,000 [Ref 4]	Grade D [Ref 2] Not Specified in operation [Ref 2] ISO 8 at rest [Ref 2]	Preferred ISO 8 at rest Controlled Not Classified (CNC) [Ref 8] Level II and Level III protection [Ref 9, 10]	Controlled Not Classified (CNC) [Ref 8] Level I Protection [Ref 9, 10]
Recommended Temperature / Humidity	Generally, [redacted] °C Generally, [redacted] % RH [Ref 6]	Generally, [redacted] °C Generally, [redacted] % RH [Ref 6]	Generally, [redacted] °C Generally, [redacted] % RH [Ref 6]	Generally, [redacted] °C Generally, [redacted] % RH [Ref 6]	Generally, [redacted] °C Generally, [redacted] % RH	Generally [redacted] °C Generally, [redacted] % RH
Filtration, Air Flow & Face Velocity/ Air Changes per hour (ACH)	Minimum HEPA Filter [Refs 4, 8] Laminar [Ref 2] OR Unidirectional [Refs 4, 6] Face Velocity [redacted] m/sec [Refs 2, 4, 6] Min [redacted] ACH [Ref 1] (Best Engineering Practice may call for [redacted]+ ACHs)	Minimum HEPA Filter [Ref 8] Mixed Flow [Ref 6] Face Velocity [redacted] m/sec [Refs 2, 4] [redacted] ACH [Refs 1, 6]	Minimum HEPA Filter [Ref 8] Mixed Flow [Ref 6] Face Velocity [redacted] [Refs 2, 6] [redacted] ACH [Refs 1, 8]	Minimum HEPA Filter [Ref 8] Mixed Flow [Ref 6] Face Velocity Not Specified [Refs 2, 6] [redacted] ACH [Ref 8]	Minimum [redacted] Filter [Ref 9, 10] Mixed Flow [Ref 6] Face Velocity Not Specified [Refs 2, 6] [redacted] ACH [Ref 8]	Minimum [redacted] Filter [Ref 9 10] Mixed Flow [Ref 6] Face Velocity Not Specified [Refs 2, 6] [redacted] ACH [Ref 8]
Differential Pressures (continuous monitoring required)	[redacted] Pa differential to adjacent rooms of different classes [Refs 2, 4] ≥[redacted] Pa [redacted]" wg) to adjacent unclassified rooms [Ref 4]	[redacted] Pa differential to adjacent rooms of different classes [Refs 2, 4] ≥[redacted] Pa ([redacted]" wg) to adjacent unclassified rooms [Ref 4]	[redacted] Pa differential to adjacent rooms of different classes [Refs 2, 4] ≥[redacted] Pa [redacted]" wg) to adjacent unclassified rooms [Ref 4]	[redacted] Pa differential to adjacent unclassified rooms [Ref 4]	[redacted] Pa differential to adjacent unclassified rooms	[redacted] Pa differential to adjacent unclassified rooms

See References on Page 4 of this Attachment.

Table II. Summary Table Environmental Monitoring Limits per Grade

NOTE: The information in this guide is presented as a guide for design of cleanrooms; it is not intended to supersede existing site procedures or environmental monitoring testing used to determine existing cleanroom standards.

LotterBhanson - C.E.C.H.S. Designation	ISO 5 / Grade A	ISO 7 / Grade B	ISO 8 / Grade C	Grade D	CNC Level 2/3	CNC Level 1
Maximum Allowed Particulate Count	**At Rest:** [redacted]/m³ > 5.0µm Ref 2 [redacted]/m³ > 0.5µm Refs 2, 5 **In Operation:** [redacted]/m³ > 5.0µm Ref 2 [redacted]/m³ > 0.5µm Refs 2,5	**At Rest:** [redacted]/m³ > 5.0µm Ref 2 [redacted]/m³ > 0.5µm Ref 2 **In Operation:** [redacted]/m³ > 5.0µm Ref 2 [redacted]/m³ > 0.5µm Refs 2, 5	**At Rest:** [redacted]/m³ > 5.0µm Ref 2 [redacted]/m³ > 0.5µm Ref 2 **In Operation:** [redacted]/m³ > 5.0µm Ref 2 [redacted]/m³ > 0.5µm Refs 2, 5	**At Rest:** [redacted]/m³ > 5.0µm Ref 2 [redacted]/m³ > 0.5µm Ref 2 **In Operation:** [redacted]	**At Rest (Preferred, Not Required):** [redacted]/m³ > 5.0µm Ref 2 [redacted]/m³ > 0.5µm Refs 2, 5 **In Operation:** Not Specified	Not Specified
Viable Counts – Airborne 90mm Settle Plate and Active Air Sampling	**Settle Plate:** < [redacted] CFU/[redacted] hrs Refs 2, 4 AND < [redacted]% Recovery Rate Ref 1 **Active Air:** < [redacted] CFU/m³ Refs 2, 4 AND < [redacted]% Recovery Rate Ref 1	**Settle Plate:** ≤ [redacted] CFU/[redacted] hrs Refs 2, 4 AND < [redacted]% Recovery Rate Ref 1 **Active Air:** ≤ [redacted] CFU/m³ Refs 2, 4 AND < [redacted]% Recovery Rate Ref 1	**Settle Plate:** ≤ [redacted] CFU/[redacted] hrs Refs 2, 4 AND < [redacted]% Recovery Rate Ref 1 **Active Air:** ≤ [redacted] CFU/m³ Refs 2, 4 AND < [redacted]% Recovery Rate Ref 1	**Settle Plate:** ≤ [redacted] CFU/[redacted] hrs Ref 2 **Active Air:** ≤ [redacted] CFU/m³ Ref 2	Not Specified	Not Specified

See References on Page 4 of this Attachment.

Table III. Summary Table Environmental Monitoring Limits per Grade (Continued)
NOTE: The information in this guide is presented as a guide for design of cleanrooms; it is not intended to supersede existing site procedures or environmental monitoring testing used to determine existing cleanroom standards.

LotterBhanson - C.E.C.H.S. Designation	ISO 5 / Grade A	ISO 7 / Grade B	ISO 8 / Grade C	Grade D	CNC Level 2/3	CNC Level 1
Viable Counts – Surface Swab or 55mm Contact Plate	< [redacted] CFU/plate [Ref 2] AND < [redacted] % Recovery Rate [Ref 1]	< [redacted] CFU/plate [Ref 2] AND < [redacted] % Recovery Rate [Ref 1]	< [redacted] CFU/plate [Ref 2] AND < [redacted] % Recovery Rate [Ref 1]	< [redacted] CFU/plate [Ref 2]	Not Specified	Not Specified
Viable Counts – Gown	< [redacted] % Recovery Rate [Ref 1]	< [redacted] % Recovery Rate [Ref 1]	[redacted] % Recovery Rate [Ref 1]	Not Specified	Not Specified	Not Specified
Viable Counts – Gloves	< [redacted] CFU/glove print [Ref 2] AND < [redacted] % Recovery Rate [Ref 1]	< [redacted] CFU/glove print [Ref 2] AND < [redacted] % recovery Rate [Ref 1]	Not Specified [Ref 2] AND < [redacted] % Recovery Rate [Ref 1]	Not Specified [Ref 2]	Not Specified	Not Specified
Maximum Testing Interval – ISO Class Microbial	Re-Classification: [redacted] months [Ref 7] Process Control: [redacted] during critical processing steps (unless not poss ble) [Ref2]	Re-Classification: [redacted] months [Ref 7] Process Control: [redacted] for ISO Grade [redacted] background areas [Ref 2] OR each shift/batch [Ref 1]	Re-Classification: [redacted] months [Ref 7] Process Control: [redacted] or Each Shift (if adjacent to ISO Grade [redacted] [Ref 1]	Re-Classification: Not Specified – recommend [redacted] months. Process Control: [redacted] [Ref 1]	Re-Classification (Preferred, Not Required): [redacted] months [Ref 7] Process Control: Not Specified	Re-Classification: Not Specified – recommend [redacted] months. Process Control: Not Specified

See References on Page 4 of this Attachment.

Table IV. Isolator/Glovebox and RABS Design Requirements

NOTE: The information in this guide is presented as a guide for design of cleanrooms; it is not intended to supersede existing site procedures or environmental monitoring testing used to determine existing cleanroom standards.

LotterBhanson - C.E.C.H.S. Designation	Isolator/RABS ISO 5 / Grade A
Other Industry Designations	Grade A [Ref 2] ISO 4.8 in operation [Ref 2] ISO 4.8 at rest [Ref 2] Class 100 [Ref 4]
Recommended Temperature / Humidity	Generally, [redacted] °C Generally, [redacted] % RH [Ref 6]
Filtration, Air Flow & Face Velocity/ Air Changes per hour (ACH)	Minimum HEPA Filter [Ref 4] Mixed, Unidirectional OR Laminar [Ref 1]; Unidirectional at Critical Points [Refs 1, 2] Velocity not Specified [Refs 1, 2] Air Changes not Specified [Refs 1, 6,8]
Differential Pressures (continuous monitoring required)	[redacted] Pa [redacted]" wg) differential to background environment [Ref 4]
Background Area Designation	Minimum ISO Grade [redacted]

LotterBhanson - C.E.C.H.S. Designation	Isolator/RABS ISO 5 / Grade A
Maximum Particulate Count	**At Rest:** [redacted] / m^3 > 5.0µm [Ref 2] [redacted] / m^3 > 0.5µm [Ref 2] **In Operation:** [redacted] /m^3 > 5.0µm [Ref 2] [redacted] / m^3 > 0.5µm [Refs 2, 5]
Viable Counts – Airborne 90mm Settle Plate and Active Air Sampling	**Settle Plate:** < [redacted] % Recovery Rate [Ref 1] **Active Air:** < [redacted] % Recovery Rate [Ref 1]
Viable Counts – Surface Swab or 55mm Contact Plate	< [redacted] % Recovery Rate [Ref 1]
Viable Counts – Gown	< [redacted] % Recovery Rate [Ref 1]
Viable Counts – Gloves	< [redacted] % recovery Rate [Ref 1]
Maximum Testing Interval	Re-Classification: [redacted] months [Ref 7] Process Control: [redacted] during critical processing steps (unless not possible) [Ref 2]

References:

1 USP General Information Chapter <1116>

2 EudraLex: The Rules Governing Medicinal Products in the European Union, Volume 4: EU Guidelines to Good Manufacturing Practice – Medicinal Products for Human and Veterinary Use, Annex 1 dated November 25, 2008

3 Parenteral Drug Association Technical Report 13 Revised, "Fundamentals of an Environmental Monitoring Program" dated June 2014

4 FDA Guidance to Industry: Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice dated September 2004

5 ISO 14644-1 Cleanrooms and Associated Controlled Environments Part 1

6 ISO 14644-4 Cleanrooms and Associated Controlled Environments Part 4

7 ISO 14644-2 Cleanrooms and Associated Controlled Environments Part 2

8 International Society of Pharmaceutical Engineers, Good Practice Guide: Heating, Ventilation, and Air Conditioning (HVAC) dated 2009

9 International Society of Pharmaceutical Engineers, Baseline Guide, Volume 1 Active Pharmaceutical Ingredients, 2nd Edition dated June 2007

10 International Society of Pharmaceutical Engineers, Baseline Guide, Volume 2 Oral Solid Dosage Forms, 2nd Edition dated November 2007