

## CLEAN ROOM MONITORING – REGULATORY STANDARDS

➤ Air Classification as per Schedule M

| Grade    | Maximum permitted number of particles / m3 equal or above |        |              |             |
|----------|---|--------|--------------|-------------|
|          | at rest   |        | in operation |             |
|          | 0.5µm   | 5.0µm  | 0.5µm        | 5.0µm       |
| <b>A</b> | 3,520   | 29     | 3,500        | 29          |
| <b>B</b> | 35,200  | 293    | 3,52,000     | 2,930       |
| <b>C</b> | 3,52,000  | 2,930  | 35,20,000    | 29,300      |
| <b>D</b> | 35,20,000   | 29,300 | not defined  | not defined |

**Note**

Grade A and B correspond to with class 100, M 3.5, ISO 5

Grade C correspond to with class 10000, M 5.5, ISO 7

Grade D correspond to with class 100000, M 6.5, ISO 8

➤ Air Classifications by USFDA guideline on Sterile Drug Products

| Clean Area Classification | <0.5 µm Particles/ft3 | <0.5 µm Particles/mt3 | Microbiological Limit |        |
|---------------------------|-----------------------|-----------------------|-----------------------|--------|
|                           |                       |                       | cfu/ft3               | cfu/m3 |
| <b>100</b>                | 100                   | 3,500                 | <1                    | <3     |
| <b>1000</b>               | 1000                  | 35,000                | <2                    | <7     |
| <b>10000</b>              | 10000                 | 350,000               | <3                    | <18    |
| <b>100000</b>             | 100000                | 3,500,000             | <25                   | <88    |

➤ Air Classifications as per WHO 2002

| Grade          | Maximum Number Permitted / M3 |        |                |
|----------------|-------------------------------|--------|----------------|
|                | Particles                     |        | Microorganisms |
|                | 0.5µm                         | 5.0µm  |                |
| <b>A (LAF)</b> | 3,500                         | 0      | <1             |
| <b>B</b>       | 3,500                         | 0      | 5              |
| <b>C</b>       | 3,50,000                      | 2,000  | 100            |
| <b>D</b>       | 3,500,000                     | 20,000 | 500            |

**Note :**

Grade A and B correspond to with class 100, M 3.5, ISO 5

Grade C correspond to with class 10000, M 5.5, ISO 7

Grade D correspond to with class 100000, M 6.5, ISO 8

➤ Airborne Classification in the European Union guide to Good Manufacturing Practice

| Grade    | Maximum Permitted Number of Particles /m <sup>3</sup> equal to or above |          |              |             |
|----------|---|----------|--------------|-------------|
|          | at rest   |          | in operation |             |
|          | >= 0.5µm  | >= 5.0µm | >= 0.5µm     | >= 5.0µm    |
| <b>A</b> | 3500  | 0        | 3500         | 0           |
| <b>B</b> | 3500  | 0        | 350000       | 2000        |
| <b>C</b> | 350000  | 2000     | 3500000      | 20000       |
| <b>D</b> | 3500000   | 20000    | not defined  | not defined |

Note :

Grade A and B correspond to with class 100, M 3.5, ISO 5

Grade C correspond to with class 10000, M 5.5, ISO 7

Grade D correspond to with class 100000, M 6.5, ISO 8

➤ **Cleanroom Environmental Monitoring**

| Sr.No. | Test  | Frequency  |
|--------|---|--|
| 1      | Particle Monitoring in air  | 6 monthly  |
| 2      | HEPA Filter Integrity Testing   | 6 monthly  |
| 3      | Air Changes Rate Calculation  | 6 monthly  |
| 4      | Air Pressure Differentials  | Daily  |
| 5      | Temperature and Humidity  | Daily  |
| 6      | Microbiological monitoring by settle plates and / or swabs in aseptic areas | Daily, and at decreased frequency in other areas |

➤ **Cleanroom Industry Design Thumb Rule**

| ISO Class | Controls       | Air Velocity at table level in FPM | Air Changes Rate per Hour | HEPA Coverage as % of Ceiling |
|-----------|----------------|------------------------------------|---------------------------|-------------------------------|
| 1         | Stringent      | 70 - 130                           | >750                      | 100                           |
| 2         | Stringent      | 70 - 130                           | >750                      | 100                           |
| 3         | Stringent      | 70 - 130                           | >750                      | 100                           |
| 4         | Stringent      | 70 - 110                           | 500 - 600                 | 100                           |
| 5         | Stringent      | 70 - 90                            | 150 - 400                 | 100                           |
| 6         | Intermediate   | 25 - 40                            | 60 - 100                  | 33 - 40                       |
| 7         | Intermediate   | 10 - 15                            | 25 - 40                   | 10 - 15                       |
| 8         | Less Stringent | 3 - 5                              | 10 - 15                   | 05 - 10                       |

➤ **Comparison between selected equivalent classes of Federal Standard 209 and ISO 14644-1**

|                  |         |          |           |            |             |              |
|------------------|---------|----------|-----------|------------|-------------|--------------|
| ISO 14644-1      | Class 3 | Class 4  | Class 5   | Class 6    | Class 7     | Class 8      |
| Classes          |         |          |           |            |             |              |
| Federal Standard | Class 1 | Class 10 | Class 100 | Class 1000 | Class 10000 | Class 100000 |

➤ Comparison of International Standards

| Country and Standard  |          |                 |                   |                         |                  |      |
|-----------------------|----------|-----------------|-------------------|-------------------------|------------------|------|
| USA 209D              | USA 209E | Britain BS 5295 | Australia AS 1386 | France AFNOR NFX 44-101 | Germany VDI 2083 | ISO  |
| Date of Current Issue |          |                 |                   |                         |                  |      |
| 1988                  | 1992     | 1989            | 1989              | 1981                    | 1990             | 1999 |
| 1                     | M 1.5    | C               | 0.035             | -                       | 1                | 3    |
| 10                    | M 2.5    | D               | 0.35              | -                       | 2                | 4    |
| 100                   | M 3.5    | E or F          | 3.5               | 4000                    | 3                | 5    |
| 1000                  | M 4.5    | G or H          | 35                | -                       | 4                | 6    |
| 10000                 | M 5.5    | J               | 350               | 400000                  | 5                | 7    |
| 100000                | M 6.5    | k               | 3500              | 4000000                 | 6                | 8    |

➤ EUGGMP 2002 Recommended Limits for Microbial Contamination

| Grade | Air Sample cfu/m <sup>3</sup> | Settle Plates Dia 90 mm cfu/m <sup>3</sup> | contact Plates Dia 55 mm cfu/m <sup>3</sup> | Glove Print 5 fingers cfu/glove |
|-------|-------------------------------|--|---|---------------------------------|
| A     | <1                            | <1   | <1  | <1                              |
| B     | 10                            | 5  | 5   | 5                               |
| C     | 100                           | 50   | 25  | -                               |
| D     | 200                           | 100  | 50  | -                               |

Note :

Grade A and B correspond to with class 100, M 3.5, ISO 5  
 Grade C correspond to with class 10000, M 5.5, ISO 7  
 Grade D correspond to with class 100000, M 6.5, ISO 8

➤ Federal Standard 209D Class Limits

| Class | Particles /ft <sup>3</sup> |           |           |           |           |
|-------|----------------------------|-----------|-----------|-----------|-----------|
|       | >= 0.1 µm                  | >= 0.2 µm | >= 0.3 µm | >= 0.5 µm | >= 5.0 µm |
| 1     | 35                         | 7.5       | 3         | 1         | NA        |

|               |     |     |     |               |     |
|---------------|-----|-----|-----|---------------|-----|
| <b>10</b>     | 350 | 75  | 30  | <b>10</b>     | NA  |
| <b>100</b>    | NA  | 750 | 300 | <b>100</b>    | NA  |
| <b>1000</b>   | NA  | NA  | NA  | <b>1000</b>   | 7   |
| <b>10000</b>  | NA  | NA  | NA  | <b>10000</b>  | 70  |
| <b>100000</b> | NA  | NA  | NA  | <b>100000</b> | 700 |

➤ **Federal Standard 209E Class Limits**

| Class Name   |         | ≥ 0.1µm |      | ≥ 0.2µm |      | ≥ 0.3µm |       | ≥ 0.5µm  |        | ≥ 5.0µm |      |
|--------------|---------|---------|------|---------|------|---------|-------|----------|--------|---------|------|
| Volume Units |         |         |      |         |      |         |       |          |        |         |      |
| SI           | English | m3      | ft3  | m3      | ft3  | m3      | ft3   | m3       | ft3    | m3      | ft3  |
| M 1          |         | 350     | 9.91 | 75.7    | 2.14 | 30.9    | 0.875 | 10.0     | 0.283  | --      | --   |
| M 1.5 1      |         | 1240    | 35   | 265     | 7.50 | 106     | 3.00  | 35.3     | 1.00   | --      | --   |
| M 2          |         | 3500    | 99.1 | 757     | 21.4 | 309     | 8.75  | 100      | 2.83   | --      | --   |
| M 2.5 10     |         | 12400   | 350  | 2650    | 75.0 | 1060    | 30.0  | 353      | 10.0   | --      | --   |
| M 3          |         | 35000   | 991  | 7570    | 214  | 3090    | 87.5  | 1000     | 28.3   | --      | --   |
| M 3.5 100    |         | --      | --   | 26500   | 750  | 10600   | 300   | 3530     | 100    | --      | --   |
| M 4          |         | --      | --   | 75700   | 2140 | 30900   | 875   | 10000    | 283    | --      | --   |
| M 4.5 1000   |         | --      | --   | --      | --   | --      | --    | 35300    | 1000   | 247     | 7.00 |
| M 5          |         | --      | --   | --      | --   | --      | --    | 100000   | 2830   | 618     | 17.5 |
| M 5.5 10000  |         | --      | --   | --      | --   | --      | --    | 353000   | 10000  | 2470    | 70.0 |
| M 6          |         | --      | --   | --      | --   | --      | --    | 1000000  | 28300  | 6180    | 175  |
| M 6.5 100000 |         | --      | --   | --      | --   | --      | --    | 3350000  | 100000 | 24700   | 700  |
| M 7          |         | --      | --   | --      | --   | --      | --    | 10000000 | 283000 | 61800   | 1750 |

➤ **ISO Standard 14644-1 Class Limits**

| ISO Classification Number | Maximum concentration limits( Particles/m3 of air) for particles equal to and larger than the considered sizes shown below |         |         |         |         |         |
|---------------------------|--|---------|---------|---------|---------|---------|
|                           | ≥ 0.1µm  | ≥ 0.2µm | ≥ 0.3µm | ≥ 0.5µm | ≥ 1.0µm | ≥ 5.0µm |
| ISO Class 1               | 10   | 2       |         |         |         |         |
| ISO Class 2               | 100  | 24      | 10      | 4       |         |         |
| ISO Class 3               | 1000   | 237     | 102     | 35      | 8       |         |
| ISO Class 4               | 10000  | 2370    | 1020    | 352     | 83      |         |
| ISO Class 5               | 100000   | 23700   | 10200   | 3520    | 832     | 29      |
| ISO Class 6               | 1000000  | 237000  | 102000  | 35200   | 8320    | 293     |
| ISO Class 7               |  |         |         | 352000  | 83200   | 2930    |
| ISO Class 8               |  |         |         | 3520000 | 832000  | 29300   |

|             |  |  |  |          |         |        |
|-------------|--|--|--|----------|---------|--------|
| ISO Class 9 |  |  |  | 35200000 | 8320000 | 293000 |
|-------------|--|--|--|----------|---------|--------|

➤ **Particles in Outdoor Air**

| Size in Microns | Number of Particles/m <sup>3</sup> on Outdoor Air |            |           |
|-----------------|---|------------|-----------|
|                 | Dirty   | Normal     | Clean     |
| >0.1            | 10000000000                                       | 3000000000 | 500000000 |
| >0.3            | 3000000000  | 900000000  | 200000000 |
| >0.5            | 300000000   | 70000000   | 10000000  |

➤ **Schedule of Mandatory Tests to Demonstrate Continuing Compliance in Cleanrooms**

| Test Parameter          | Class       | Maximum Time Interval |
|-------------------------|-------------|-----------------------|
| Particle Count Test     | <= ISO 5    | 6 months              |
|                         | > ISO 5     | 12 months             |
| Air Pressure Difference | All Classes | 12 months             |
| Airflow                 | All Classes | 12 months             |

➤ **Schedule of Optional Tests to Demonstrate Continuing Compliance in Cleanrooms**

| Test Parameter           | Class       | Maximum Time Interval |
|--------------------------|-------------|-----------------------|
| Installed Filter Leakage | All Classes | 24 months             |
| Containment Leakage      | All Classes | 24 months             |
| Recovery                 | All Classes | 24 months             |
| Airflow Visualization    | All Classes | 24 months             |

➤ **Special Requirements for ISO Class 3 Cleanrooms**

| Special Requirements for ISO Class 3 Cleanrooms |   |
|---|---|
| Air Quality                                     | Total Hydrocarbons <1 ppm; Na <0.1 µg/m <sup>3</sup>    |
| Fresh Air Intake                                | 0.5 m <sup>3</sup> /min per sqm of cleanroom floor area |
| Vibration                                       | <0.1 µ ( Building); <0.01 µ ( Equipment) rms            |
| Noise   | < 55 dbA  |
| Temperature                                     | .1 degree C   |
| Humidity  | < 2%  |
| Magnetic field var                              | < 1 mG  |
| Static charge                                   | < 50 v  |

➤ **Types of Operations for Aseptic Preparations**

Grade                      Types of Operations for Aseptic Preparations

- A** Aseptic preparation and filling
- B** Background room conditions for activities requiring Grade A
- C** Preparation of Solution to be filtered
- D** Handling of components after washing

**Note :**

**Grade A and B correspond to with class 100, M 3.5, ISO 5**  
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