

# CLASSIFICATION OF CLEANROOMS

## Introduction

This paper describes the classification of clean rooms comparing a number of international standards, as well as discussing classifications in common use within New Zealand.

A Clean Room or Clean Space is defined as a room or suite of rooms or an area of controlled environment in which the concentration of airborne particulate matter is strictly controlled and where other factors may be controlled within limits necessary to cater for particular needs<sup>1</sup>.

The use of clean spaces for manufacture, packaging, laboratories and research has traditionally been the domain of the pharmaceutical, biotechnology, semi-conductor, microelectronics, and aerospace industries, however application to other sectors is becoming more prevalent.

Materials research, manufacture and packaging of certain food products, optic applications, and paint/surface finish industries also require conditions where particulates and particulate contamination are controlled.

Hospital theatres utilise similar design and operation principles to clean rooms, however the objective with such facilities is to control particular types of contamination, rather than the quantities of particles present.

## Clean Room Standards

There are a number of International Standards defining "Clean Rooms". These are commonly referenced in the biotechnology, pharmaceutical, microelectronics, and other sectors. The benchmark international clean room standards are:

- US Federal Std 209E 1992
- EEC cGMP 1989
- France AFNOR 1989
- German VDI 2083 1990
- British BS 5295 1989
- Japan JIS B 9920 1989
- ISO EN 14611-1 1999

Closer to New Zealand, Australia has published a standard dealing with the classification of air cleanliness and general principles of clean space control. This standard is AS 1386 : 1989. It is based on a metric system of classification for clean spaces. AS 1386 is used by a number of New Zealand companies as a reference for design and operation of cleanrooms.

AS 1386 has seven parts. There is an associated standard AS 1807 : 1989, a multi-part standard which lists the methods of test and apparatus for clean space testing.

The content of both of these standards is typical of the international standards for clean rooms and is summarised below:

**Part 1:** *Principles of Clean Space Control (AS 1386.1)*

Sets out the principles of clean space control. Six classes of air cleanliness are specified and guidelines are given for the selection of airflow patterns, control of temperature and humidity, regulation of air pressure, materials and construction techniques, as well as operating procedures. Clean spaces may be achieved in rooms, or in workstations or safety cabinets within a room.

**Part 2:** *Laminar Flow Cleanrooms (AS 1386.2)*

Specifies requirements for laminar flow cleanrooms, with a minimum air cleanliness of Class 3.5 in accordance with AS 1386.1.

**Part 3:** *Non-laminar Flow Cleanrooms - Class 350 and Cleaner (AS 1386.3)*

Specifies requirements for non-laminar flow cleanrooms with a minimum air cleanliness of Class 350 in accordance with AS 1386.1.

- Part 4: Non-laminar Flow Cleanrooms - Class 3500 (AS 1386.4)*  
Specifies requirements for non-laminar flow cleanrooms with an air cleanness of Class 3500 in accordance with AS 1386.1.
- Part 5: Clean Workstations (AS 1386.5)*  
Specifies requirements for clean workstations.
- Part 6: Operation and Inspection of Cleanrooms (AS 1386.6)*  
Sets out recommendations and requirements for the operation and inspection of laminar flow cleanrooms and non-laminar flow cleanrooms. Reference is made to three distinct stages of qualification for cleanrooms (as-built cleanroom, at rest cleanroom and operational cleanroom).
- Part 7: Installation and Use of Clean Workstations (AS 1386.7)*  
Sets out recommended practices for installation, operation, maintenance and inspection of clean workstations (laminar flow) specified in AS 1386.5.

AS 1807 describes the apparatus and test methods for determining specific performance attributes for clean rooms and clean workspaces. The standard defines 25 Methods of Test.

- 1807.0 Apparatus
- 1807.1 Determination of air velocity and uniformity of air velocity in clean rooms
- 1807.2 Determination of performance of clean workstations and laminar flow safety cabinets under loaded filter conditions
- 1807.3 Determination of air velocity and uniformity of air velocity in laminar flow cleanrooms
- 1807.4 Determination of performance of laminar flow cleanrooms under loaded filter conditions
- 1807.5 Determination of work zone integrity
- 1807.6 Determination of integrity of terminally mounted HEPA filter installations
- 1807.7 Determination of integrity of HEPA filter installations not terminally mounted
- 1807.8 Particle counting in work zone by automatic particle counter
- 1807.9 Particle counting in cleanrooms by microscopic sizing and counting
- 1807.10 Determination of air pressure in clean rooms
- 1807.11 Determination of airflow parallelism in laminar flow clean rooms
- 1807.12 Determination of temperature in work zones
- 1807.13 Determination of relative humidity in cleanrooms
- 1807.15 Determination of illuminance
- 1807.16 Determination of sound level in clean rooms
- 1807.17 Determination of vibration in clean rooms
- 1807.18 Determination of vibration in workstations and safety cabinets
- 1807.19 Sizing and counting of particulate contaminants in and on clean room garments
- 1807.20 Determination of sound level at installed workstations and safety cabinets
- 1807.21 Determination of inward air velocity of class 1 biological safety cabinets
- 1807.22 Determination of air barrier containment of laminar flow safety cabinets
- 1807.23 Determination of intensity of radiation from germicidal ultraviolet lamps
- 1807.24 Determination of recovery times of clean rooms
- 1807.25 Determination of gas tightness of outer shell of biological safety cabinets

## Clean Room Classifications

Typically a clean room will be specified by a classification from one of the international standards above. The classification relates to the definition of a maximum allowable number of particles of a range of sizes, related to a standard volumetric sample size.

Various classification classes are stated based on these limits. There is co-relation between the classifications used by various standards authorities. Table 1 presents a comparison of the US, EEC, French, German, British, Japanese and ISO classes.

A comparison of the Australian (metric) classification system to the US imperial system is given in Table 2. (The figures are rounded after conversion as  $1.0 \text{ m}^3 = 35.315 \text{ ft}^3$ )

Table 1 –Air Classification for International Cleanroom Standards<sup>2</sup>

Approximate Particles per m <sup>3</sup> ≥0.5 mm	US 209E 1992	US 209E Imperial equivalent	EEC CGMP 1989	France AFNOR 1989	Germany VDI 2083 1989	Britain BS 5295 1989	Japan JIS B 9920 1989	ISO EN 14644-1 1999
1								
3.5					0		2	2
10	M 1							
35	M 1.5	1			1		3	3
100	M 2							
353	M 2.5	10			2		4	4
1 000	M 3							
3 530	M 3.5	100	A + B	4 000	3	E or F	5	5
10 000	M 4							
35 300	M 4.5	1 000			4	G or H	6	6
100 000	M 5							
353 000	M 5.5	10 000	C	400 000	5	J	7	7
1 000 000	M 6							
3 530 000	M 6.5	100 000	D	4 000 000	6	K	8	8
10 000 000	M 7							
100 000 000	M 7.5	1 000 000		40 000 000		L	9	9

Table 2- Comparison of Australian (metric) and US (imperial) Cleanroom Standards<sup>3</sup>

Class of Air Cleanliness		Maximum number of particles per litre (metric system) and per cubic foot (U.S. System)									
		Particle size µm									
		0.1 µm and larger		0.2 µm and larger		0.3 µm and larger		0.5 µm and larger		5 µm and larger	
Metric	U.S.	Metric	U.S.	Metric	U.S.	Metric	U.S.	Metric	U.S.	Metric	U.S.
0.035	1	1.25*	35	0.265	7.5	0.1	3	0.035	1	N/A	N/A
0.35	10	12.5*	350	2.65	75	1	30	0.35	10	N/A	N/A
3.5	100	N/A	N/A	26.5	750	10‡	300	3.5	100	N/A	N/A
35	1000	N/A	N/A	N/A	N/A	N/A	N/A	35	1000	0.25	7
350	10000	N/A	N/A	N/A	N/A	N/A	N/A	350	10000	2.5	70
3500	100000	N/A	N/A	N/A	N/A	N/A	N/A	3500	100000	25	700

### LEGEND

- \* Rounded Up
- ‡ Rounded Down
- N/A Not Applicable

## Air Classifications for Good Manufacturing Practice (GMP)

Within many industry sectors, codes of Good Manufacturing Practice or cGMPs are in place. The way in which clean rooms are defined varies between sectors. Some cGMPs specify air minimum air classifications, for instance those dealing with aseptic or sterile manufacture; others call for air quality “appropriate” to the activity. This is generally dictated by current best practice within the industry.

In New Zealand, both the MoH and MAF make use of cGMPs of the latter type for medicines, agricultural compounds, veterinary products, dietary supplements, and broader “therapeutic/biotech” products. For food, dairy and similar facilities, MAF’s current practice is to classify facilities based on the grade of air filtration used for treatment of incoming air.

The latter practice does not allow the classification of the clean space to an internationally recognised standard, as filtration of a specified grade will produce air quality dependant on the ambient particulate and airflow conditions. Hence an anomaly currently exists in the understanding of what constitutes a “clean room” within New Zealand.

Australian regulatory authorities tend to approach clean room classification in a more prescriptive manner. For example the Therapeutic Goods Administration (TGA) who administer the cGMP for facilities undertaking manufacture of therapeutic goods in Australia specify a minimum air quality in their code.

As Australian cGMPs have some influence on New Zealand organisations, it is appropriate to consider this position. Currently the TGA regulations encompass far more products than their New Zealand equivalent. Their applicability includes dietary supplements, complimentary medicines, vitamins, cosmetics, sunscreen, some herbal products and health foods in the broader “therapeutic” category.

The TGA reference the Australian Standard in cGMPs but recognise that the lowest air cleanliness class in common use (class 3500) is often an excessive minimum requirement for a “clean room” intended for use in the manufacture or packaging of low-risk products.

The Australian cGMP for Therapeutic Goods provides for a class of air defined as “Class 7000” as being appropriate for this type of activity. Part 1, clause 115 of the code of GMP defines Class 7000 air as:

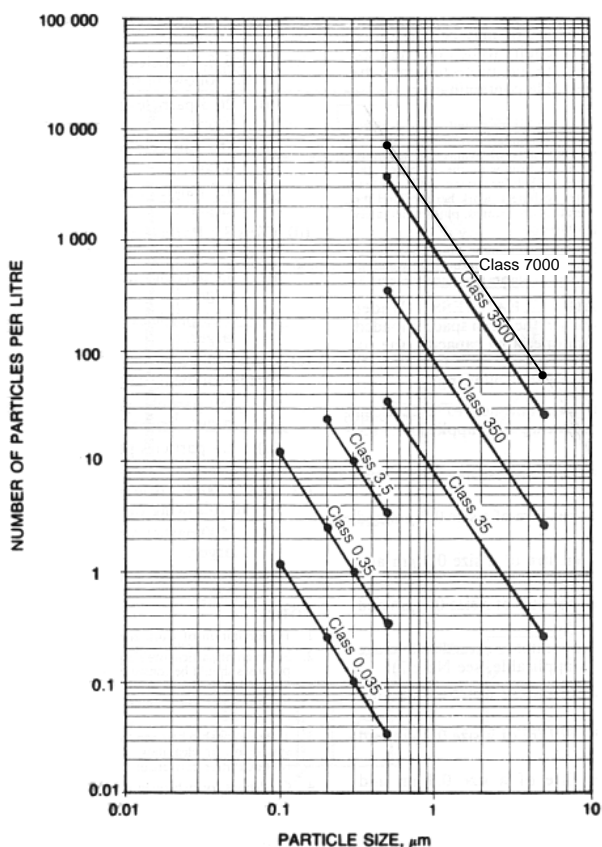
*“The air so supplied is likely to be equal to or better than the equivalent of “Class 7000” (approximately 300 particles of 2 micrometres particle size per litre) as extrapolated from AS 1386 : 1989: Cleanrooms and Clean Workstations.”<sup>4</sup>*

There is no mention of Class 7000 in AS 1386. The cGMP extrapolates from the metric system for air cleanliness to define an air quality deemed appropriate for therapeutic applications, which equates to ½ of class 3500.

From Table 2 it can be seen that Class 7000 approximates to no more than 7000 particles of 0.5 microns or larger per litre, and no more than 50 particles of 5 microns or larger per litre. The relationship between particle size distributions can be seen from Figure 1.

AS 1386 does not specify acceptable limits for micro-organisms in the various classes of clean room. This approach is consistent with international standards of the similar type. The New Zealand and Australian cGMPs discussed do not specify limits either. There is however a requirement to run programs to monitor and control microbial contamination where protection is required and set limits commensurate with the results of these programs.

Figure 1 – Particle Size Distribution for Clean Rooms<sup>4</sup>



## Air Classification Testing

Testing is required by all clean room standards to assure compliance with air classification is achieved and maintained. This can be achieved by a number of methods. The most common method in use is to sample the environment using a proprietary automatic air sampler. A number of companies within New Zealand provide such a service.

Standards for clean room monitoring require assessment of number of particles over a range of at least 2 sizes. For lower classification clean rooms it is common to use 0.5µm and 5µm as the range reported. For Class 7000, given the reference to the 2 micron particle size it is appropriate to report this size also, but not essential, provided 0.5 and 5 microns are reported.

An important aspect of testing clean rooms for the purpose of classification is consideration of the activity to be undertaken within the area. Internal contamination or disturbances within a clean space can be generated by raw materials/goods movement, personnel working or moving within the area, service equipment, or the operation of the intended process itself.

Therefore within any air class, it could be possible for three states to exist, each with potentially some effect on air quality. These are:

1. Clean space commissioned but without equipment installed (empty space or as-built).
2. Clean space completely fitted out and operational, without personnel movement (at rest).
3. Clean space fully operational under normal or worst case conditions (fully operational or dynamic).

For spaces classified cleaner than AS 1386/Class 3500, It is mandatory to conduct testing under fully operational conditions. However the standard allows for spaces of Class 3500 and lower to be tested either at rest or empty. This decision can have a significant effect on the design of facilities and ongoing compliance cost. Assessment of the most appropriate solution will depend on the airflow dynamics of the clean space, the process/product in question, and regulatory authority or industry best practice.

## Composition of Particulate Contamination

Dust particles in the air differ not only in regard to their chemical composition, but also their size. Location and ambient condition has a significant influence on the composition of air in the environment.

Much work has been undertaken to characterise air quality for design purposes. In one study statistics for “normally polluted city air”<sup>5</sup> show that typically, two distinct ranges of particle size occur.

1. Particles greater than 2-5 $\mu$ m, typically of natural origin from fields, soil, gardens etc. Chemical assay typically detects elements such as silicon, potassium, magnesium, iron etc.
2. Particles less than 2.5-5 $\mu$ m, typically of inorganic origin from traffic and industrial emissions, combustion exhaust and the like. These particulates generally contain carbon solids, sulphur etc.

ASHRAE<sup>6</sup> defines particles smaller than 2.5 $\mu$ m in diameter as fine mode and those larger than 2.5  $\mu$ m as coarse mode. Fine mode particles generally are less likely to settle in ambient conditions and are just as likely to deposit on vertical surfaces as on horizontal surfaces. Coarse mode particles will generally settle, and thus have a shorter lifetime in the airborne state.

Control of airborne micro-organisms is often a concern in clean space design. These can usually be distinguished as fungi, bacteria, spores or viruses, with an ability to multiply and grow. Typically bacteria, fungi and spores have a size of greater than 0.5 $\mu$ m and can be attached to dust particles in groups.

The number of micro-organisms present in atmospheric air varies according to wind speed, temperature humidity and location. Values between 200 and 2000 micro-organisms per m<sup>3</sup> have been reported in some studies<sup>5</sup>.

## Control of Particulate Contamination

For Clean Spaces Class 3500 and lower - Control of ambient particulates and airborne micro-organisms is primarily achieved using air filtration techniques. This is the most common clean space classification found in New Zealand and Australia at the present time.

Major factors influencing filter design and selection include air cleanliness required, the specific particle size range requiring filtration and resistance to airflow through the filter. The effect of velocity of the air stream is negligible over the range of flow generally used for conditioned air systems.

Filter efficiency, is the characteristic that determines the air cleanliness which will be achieved from a particular air stream. Efficiency is the ability of the filter to remove particulate matter from an air stream. The efficiency of many dry-type filters increases with dust load, so the initial (clean filter) efficiency should be considered for design in applications with low dust concentrations.

Airflow resistance (or simply resistance) is the static pressure drop across the filter at a given airflow rate. Dust-holding capacity defines the amount of a particular type of dust that an air cleaner can hold when it is operated at a specified airflow rate to some maximum resistance value or before its efficiency drops seriously as a result of the collected dust.

Air Filters are classified by their efficiency in a number of ways to take account of the varying behaviours of fine and course particles. The common test methods and classifications used have been DIN 24 184/5, Eurovent 4/5 and ASHRAE 52-76. Recently EN 779 was introduced to harmonise standards. The methods commonly used to classify filter efficiency<sup>7</sup> are: -

### Arrestance

A measure of a filter to collect a standard dispersed synthetic dust. This filter test is particularly suited to low- and medium-efficiency air filters. It does not distinguish between filters of higher efficiency. This type of efficiency measurement is called synthetic dust weight arrestance to distinguish it from other efficiency values

### Dust-Spot Efficiency

A measure of the ability of a filter to reduce the soiling of fabrics and surfaces. These effects depend mostly on fine particles, so this test most useful for high-efficiency filters. This test may cause a low efficiency filter to test at different efficiencies at different locations or times.

### Fractional Efficiency or Penetration

This test uses uniform particle size aerosols and produces an accurate measure of the particle size versus efficiency characteristic of a filter. The method is time-consuming however, the dioctylphthalate (DOP) test for High Efficiency Particulate Air (HEPA) filters is widely used.

### Particle Size Efficiency.

Atmospheric dust is fed to the filter, and air samples taken upstream and downstream by particle counter to obtain efficiency versus particle size. Several manufacturers publish efficiencies for a size range of atmospheric dust. No test standard currently exists for Particle Size Efficiency Testing.

In order to design an appropriate filtration strategy to achieve clean room classification, it is necessary to consider the ambient inlet air condition and the air classification required. This is particularly relevant in situations where lower air classes are specified, or where processing equipment is being modified to meet particular specifications. It is also an important consideration in the design of pre-filtration for HEPA filters to maximise their operating life and installation costs.

Often a filtration solution will be targeted at particles of a particular size present in proportionately high concentrations in a specific air stream. In this case a fractional efficiency calculation is required such that the concentration (C) of the fugitive particles are reduced to an acceptable level. The formula below applies

$$T(x) = \frac{C_{in}(x) - C_{out}(x)}{C_{in}(x)}$$

where

$T(x)$  = Efficiency of air filter required.

$C_{in}(x)$  = Concentration of inlet dust particles of interest

$C_{out}(x)$  = Concentration of outlet dust particles of interest

## Summary

Numerous international standards exist for the classifications of clean spaces. The classifications for various standards can be related to each other for the purposes of comparison and show some correlation. In New Zealand, the Australian Standard AS 1386 : 1986 is commonly used to classify clean spaces. This standard defines a metric equivalent to common international classifications.

There is a growing trend in the food, dietary supplement and complimentary medicines sectors to manufacture and package product in clean spaces. For such applications the lowest clean space classification to internationally accepted standards is considered by regulators to be excessive for many “low-risk” applications.

An extrapolation from Class 3500, the lowest in the Australian standard has been mandated by an Australian regulatory authority as appropriate for such situations. This air classification can be defined and measured based on particle size distribution in air supplies in a similar manner to standard clean spaces. In such applications it is also appropriate to consider the operational status of the clean space and the effect that personnel and goods movement, equipment layout and processing may have on the classification or the process.

Specification of a clean space purely based on filtration specification or grade does not guarantee a clean space will comply with international standards. Incoming dust concentrations and characteristics must be considered and filters of appropriate efficiency and capacity selected to ensure concentrations of particulates are controlled and installations perform efficiently.

## References

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