

ISO 14644-1:2015 Revisions Summary

GUEST SPEAKER

Mrs. Chris Wang
Asia GMP Expert /Senior Marketing Manager
Life Science Industry – China
Particle Measuring Systems

customerservice@pmeasuring.com.sg

What Is ISO 14644?

ISO 14644 represents the most used standards in Pharma and Electronics controlled environments.

- ISO 14644-1 specifies classes of air cleanliness in terms of the number of particles expressed as a concentration in air volume.
- It also specifies the standard method of testing to determine cleanliness class, including selection of sampling locations.

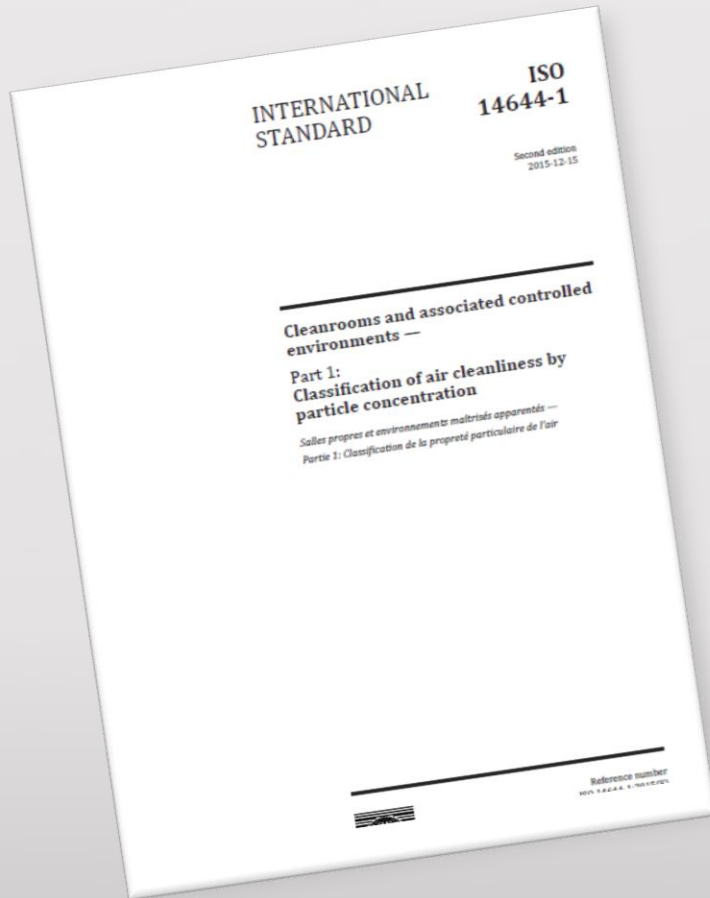


What Is ISO 14644?

ISO 14644 consists of the following parts, under the general title ***Cleanrooms and associated controlled environments:***

- Part 1: Classification of air cleanliness by particle concentration
- Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration
- Part 3: Test methods
- Part 4: Design, construction and start-up
- Part 5: Operations
- Part 7: Separative devices (clean air hoods, gloveboxes, isolators and mini-environments)
- Part 8: Classification of air cleanliness by chemical concentration (ACC)
- Part 9: Classification of surface cleanliness by particle concentration
- Part 10: Classification of surface cleanliness by chemical concentration

Introduction



- The recent revision of ISO 14644-1 and-2 has introduced several changes for cleanroom classification and monitoring guidelines.
- The ISO community voted in favor of this revision on October 29th, 2015.
- This presentation discusses those changes and how they affect you.

New 14644-1:2015 Revision Summary and Purpose



Notable areas of change:

1. Sample Location Number
2. Particle Concentration Limit
3. Particle Counter Calibration

New 14644-1:2015 – Sample Location

How to determine the sample location number:

- A new table has been developed for the determination of the number of sample locations, replacing “*Location Number* = $\sqrt{m^2 \text{room area}}$ ” from the ISO 14644-1:1999 version of the standard.
- For all room sizes above 6 m², the new table results in an increase of required sample locations.
- The ISO14644-1:1999 standard required the UCL 95% (Upper Confidential Limit) calculation for sample locations to be between 2 and 9.

New 14644-1:2015 Sample Location Table

What this means to you:

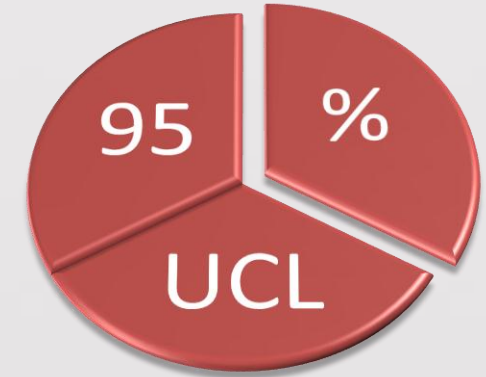
- Sample location number calculations(*) are now unnecessary.
- * For all Cleanrooms *Smaller* than 1000m² use the table.
- * For all Cleanrooms *Bigger* than 1000m² use Formula A.1.

Formula A.1:

$$N_L = 27 \times \left(\frac{A \text{ m}^2}{1000} \right)$$

Area of zone [m2]	ISO 14644-1:1999	ISO 14644-1:2015
2	2	1
4	2	2
6	3	3
8	3	4
10	4	5
24	5	6
28	6	7
32	6	8
36	6	9
52	8	10
56	8	11
64	8	12
68	9	13
72	9	14
76	9	15
104	11	16
108	11	17
116	11	18
148	13	19
156	13	20
192	14	21
232	16	22
276	17	23
352	19	24
436	21	25
636	24	26
1000	32	27
>1000	n/a	See Formula A. 1

New 14644-1:2015 – Sample Location



- The new table has been pre-calculated to eliminate the need for this calculation.
- The new method, when successfully applied, assures that at least 90% of the room is compliant at a 95% confidence limit.

The determination of each sampling location will be based on a semi-random sampling technique, derived from "hypergeometric" distribution, which is the statistical model for sampling without replacement.


ISO 14644-1:1999 – Maximum Concentration Limits

Table 1 Selected airborne particulate cleanliness classes

ISO 14644-1:1999 Classification Number (N)	Maximum concentration limits (particles/m ³)					
	0.1 µm	0.2 µm	0.3 µm	0.5 µm	1.0 µm	5.0 µm
ISO Class 1	10					
ISO Class 2	100	24	10			
ISO Class 3	1 000	237	102	35		
ISO Class 4	10 000	2 370	1 020	352	83	
ISO Class 5	100 000	23 700	10 200	3 520	832	29
ISO Class 6	1 000 000	237 000	102 000	35 200	8 320	298
ISO Class 7				352 000	83 200	2 930
ISO Class 8				3 520 000	832 000	29 300
ISO Class 9				35 200 000	8 320 000	293 000

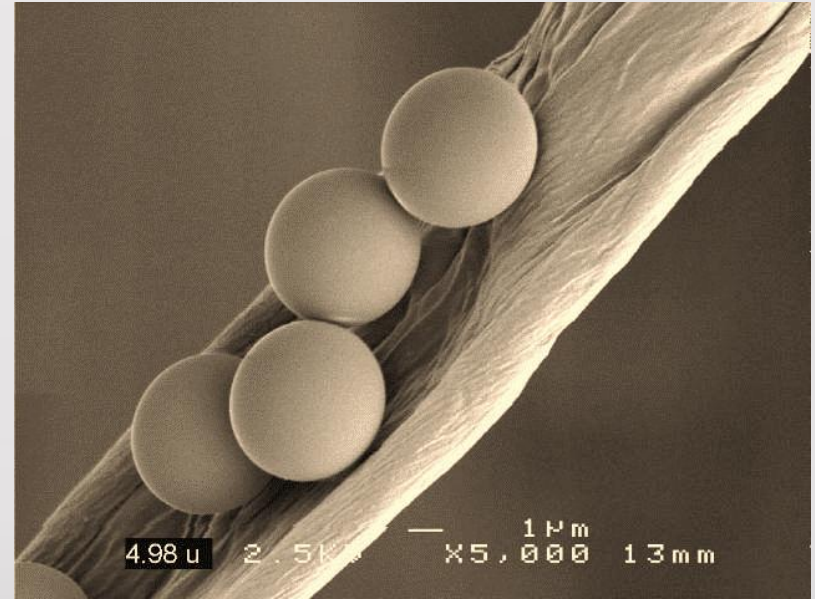
ISO 14644-1:2015 – New Maximum Concentration Limits

Table 1 Selected airborne particulate cleanliness classes

ISO 14644-1:2015 Classification Number (N)	Maximum concentration limits (particles/m ³)					
	0.1 µm	0.2 µm	0.3 µm	0.5 µm	1.0 µm	5.0 µm
ISO Class 1	10					
ISO Class 2	100	24	10			
ISO Class 3	1 000	237	102	35		
ISO Class 4	10 000	2 370	1 020	352	83	
ISO Class 5	100 000	23 700	10 200	3 520	832	
ISO Class 6	1 000 000	237 000	102 000	35 200	8 320	298
ISO Class 7				352 000	83 200	2 930
ISO Class 8				3 520 000	832 000	29 300
ISO Class 9				35 200 000	8 320 000	293 000

ISO 14644-1:2015 – Concentration Limit Considerations

- The ISO 14644-1:2015 is now the same as the old US Fed Std 209E in the treatment of 5 micron particles in ISO Class 5 (old FS 209E class 100).
- This change was largely influenced by US expert argument.



5 µm PSLs on a cotton fiber

ISO 14644-1:2015 – Concentration Limit Changes

- The new revision of ISO 14644-1 leaves a gap in classification of Grade A and B (at rest) in Annex 1 of the EU GMP, as well as PIC/S, WHO, Japanese and China GMP guidance for sterile products. Limits are provided to be between 20 and 29 parts/m³.
- To deal with this problem, ISO 14644-1:2015, Annex C7, introduces the use of the macro-particle descriptor 'M', which can be used to describe either the specified or measured concentration of macroparticles $\geq 5 \mu\text{m}$.



New ISO 14644-1:2015 Instrument Calibration Requirements

B.2.2 Instrument calibration

The instrument shall have a valid calibration certificate; the frequency and method of calibration should be based on current accepted practice.

14644-1:1999

A.2.2 Instrument calibration

The particle counter shall have a valid calibration certificate: the frequency and method of calibration should be based upon current accepted practice as specified in [ISO 21501-4](#).^[2]

14644-1:2015

NOTE Some particle counters **cannot be calibrated** to all of the required tests in [ISO 21501-4](#). If this is the case, record the decision to use the counter in the test report.

What this means to you:

You are expected to have instruments calibrated in accordance with ISO requirements.

Use of non **ISO21501-4** compliant instruments will require additional and **undesirable** explanations to authorities.

ISO-21501 – Why Is It Important?

- The ISO 14644-1:2015 introduces the need of ISO 21501-4 particle counters, which assure all cleanroom certification is based on verified data accuracy and reliability.
- Cleanroom users shall then look to ISO 21501 as a method to meet cGMP, EU GMP, ISO 14644-1, and other requirements.
- This change to the ISO 14644-1 represents an important step in improving the accuracy of clean room contamination evaluation and aseptic process control.



Summary

- The new changes described here will impact cleanroom classifications, and any company that needs to comply with this standard will be required to update their internal SOP in order to meet the new ISO 14644 requirements.
- ISO 14644-1:2015 was published on November 1st 2015 and is effective since December 15, 2015. All users who want to be compliant with this standard will be required to take any necessary action before the end of 2016.