UPDATED ISO 14644 1 & 2

- **Short background**
- **Main changes in ISO 14644-1**
- **Main changes in ISO 14644-2**
- **Q & A**

- US Federal Standard 209E Airborne Particulate Cleanliness Classes in Cleanrooms and Clean Zones – Fed Std 209E published June 16, 1988
- Over time, the industry requirements for single standard for classification & testing, lead to the formation of ISO 14644 series.
- Cancelation of 209E standard was official on November 29, 2001. The cancelation statement stated:

"…recommended that International Standard **ISO 14644**, Cleanrooms and controlled environments-Part 1: Classification of air cleanliness, and Part 2: Specifications for testing and monitoring to prove continued compliance with ISO 14644-1, **supersede FED-STD-209E**."

NOTICE OF CANCELLATION FED-STD-209 NOTICE 1
November 29, 2001

FEDERAL STANDARD

AIRBORNE PARTICULATE CLEANLINESS CLASSES
IN CLEANROOMS AND CLEAN ZONES

Federal Standard 209E dated September 11, 1992 is hereby canceled and superseded by International Organization for Standardization (ISO) Standards. International Standards for Cleanrooms and associated controlled environments, ISO 14644-1 Part 1: Classification of air cleanliness; and ISO 14644-2 Part 2: Specifications for testing and monitoring to prove continued compliance with ISO 14644-1. Application for copies of ISO Standards 14644-1 Part 1, and 14644-2 Part 2; may be addressed to the Institute of Environmental Sciences and Technology (IEST), 940 East Northwest Highway, Mount Prospect, IL 60056-3444. Phone: 847-255-1561, Fax: 847-255-1699, Web site: www.iest.org, E-mail: publicationsales@iest.org.

Preparing Activity: GSA-FSS
FSC 3694

ISO 14644 series

Former	Current
• ISO 14644-1: Classification of air cleanliness	• ISO 14644-1: Classification of air cleanliness **by particle concentration**
• ISO 14644-2: Specifications for testing and monitoring to prove continued compliance with 14644 -1	• ISO 14644-2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration

ISO 14644 series

Current

- ISO 14644-3 (2005):
  Test methods
- ISO 14644-4 (2001):
  Design, construction and start up
- ISO 14644-5 (2004):
  Operations
- ISO 14644-7 (2004):
  Separative devices (clean air hoods, gloveboxes, isolators, minienvironments)

Main changes in ISO 14644-1

Main changes in ISO 14644-1

ISO 14644-1:2015 – New maximum concentration limits

Table 1 — ISO Classes of air cleanliness by particle concentration

ISO Class number (*N*)	Maximum allowable concentrations (particles/m³) for particles equal to and greater than the considered sizes, shown below[a]					
	0,1 µm	0,2 µm	0,3 µm	0,5 µm	1 µm	5 µm
1	*10*[b]	d	d	d	d	e
2	100	*24*[b]	*10*[b]	d	d	e
3	1 000	237	102	*35*[b]	d	e
4	10 000	2 370	1 020	352	*83*[b]	e
5	100 000	23 700	10 200	3 520	832	d, e, f
6	1 000 000	237 000	102 000	35 200	8 320	293
7	c	c	c	352 000	83 200	2 930
8	c	c	c	3 520 000	832 000	29 300
9[g]	c	c	c	35 200 000	8 320 000	293 000

Reference FDIS 14644-1:2015

Main changes in ISO 14644-1

ISO 14644-1:2015 – New maximum concentration limits:

d Sampling and **statistical** limitations for particles in low concentrations make classification inappropriate

e Sample collection limitations for both particles in low concentrations and sizes greater than 1 µm make classification at this particle size inappropriate, due to **potential particle losses** in the sampling system

F In order to specify this particle size in association with ISO Class 5, the **macroparticle descriptor M** may be adapted and used in conjunction with at least one other particle size

Main changes in ISO 14644-1

ISO 14644-1:2015 – Sample locations & number of samples

The most significant change is the adoption of a more consistent statistical approach to the: (1) selection and the (2) number of sampling locations; and the evaluation of the data collected.

The new approach allows each location to be treated independently with at least a 95 % level of confidence that at least 90 % of the cleanroom or clean zone areas will comply with the maximum particle concentration limit for the target class of air cleanliness.

The new method eliminate the need for UCL (95%) calculation !

Main changes in ISO 14644-1

ISO 14644-1:2015 – Sample locations & number of samples

(2) Number of required samples:

The former version (ISO 14644-1:1999) minimum number of sample locations was determined using the following equation

$$\text{Location number} = \sqrt{Room\ area\ in\ m^2}$$

$N_{L=\sqrt{A}}$

N_L- is the minimum of sampling locations (rounded up to a whole number)

A- is the area of clean room. Clean zone in square meter

Main changes in ISO 14644-1

ISO 14644-1:2015 – Sample locations & number of samples

(2) Number of required samples:

New lookup table has been developed for the determination of the number of sample locations

For all room sizes above 6 m^2, the new table results in an **increase** of required sample locations ;

Table A.1 — Sampling locations related to cleanroom area

Area of cleanroom (m^2) less than or equal to	Minimum number of sampling locations to be tested (N_L)
2	1
4	2
6	3
8	4
10	5
24	6
28	7
32	8
36	9
52	10
56	11
64	12
68	13

Main changes in ISO 14644-1

ISO 14644-1:2015 – Sample locations & number of samples

(1) Sample location selection:

No assumptions are made regarding the distribution of the actual particle counts over the area of the cleanroom or clean zone;

In ISO 14644-1:1999 an underlying assumption was that the particle counts follow <u>the same normal distribution</u> across the room;

In ISO 14644-1:2015 this assumption has been discarded to allow the sampling to be used in rooms, where the particle counts vary in a more complex manner.

Main changes in ISO 14644-1

ISO 14644-1:2015 – Sample locations & number of samples

(1) Sample location selection:

The determination of each sampling **location** is based on a semi-random sampling technique, based on a "hypergeometric" distribution.

Revised sampling maps should be issued!

Main changes in ISO 14644-1

ISO 14644-1:2015 – Sample locations & number of samples

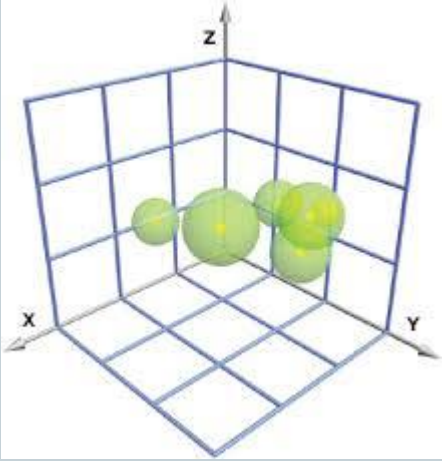
(1) Sample location selection:

In order to position sampling locations:

a) Use the minimum number of sampling locations N_L derived from the lookup table.
b) Then divide the whole cleanroom or clean zone into N_L sections of equal area
c) Select within each section a sampling location considered to be representative of the characteristics of the section, and
d) At each location, position the particle counter probe in the plant of the work activity or another specified point

Main changes in ISO 14644-1

ISO 14644-1:2015 – Sample locations & number of samples



Use:

- ✓ Cleanroom layout – including operation equipment
- ✓ Known operation working positions
- ✓ HVAC system elements: clean air entrance or filters positioning, return air grills

Justify selected locations ☺

Main changes in ISO 14644-1

ISO 14644-1:2015 – Sampling counter calibration

The particle counter shall have a valid calibration certificate:

The frequency and method of calibration should be based upon current practice as specified in **ISO 21501-4**

Main changes in ISO 14644-1

Issues not included in this presentation:

- Intermediate decimal cleanliness classes and particle size thresholds
- Airborne particle concentration evaluation. Performing more than one sample per location.
- Out-of-specification result (ISO 14644-2 to be issued as alert/action levels)

Main changes in ISO 14644-2

Main changes in ISO 14644-2

Potential benefits gained from monitoring are:

- ✓ faster response to adverse events and conditions,
- ✓ ability to develop trends from data over time,
- ✓ integration of data from multiple instruments,
- ✓ enhanced knowledge of installation and process, which allows for more effective risk assessment, and
- ✓ improved control of operational costs and product losses.

Main changes in ISO 14644-2

ISO 14644-2:2015 – Risk Assessment

A risk assessment shall be undertaken in order to:

- ✓ Develop a monitoring plan by determining factors that may affect the ability to maintain the agreed air cleanliness.
- ✓ Determine the monitoring requirements to provide evidence of performance.

Main changes in ISO 14644-2

ISO 14644-2:2015 – Risk Assessment

The assessment should include performance & operation monitored factors as:

- Contamination sources and their impact on manufacturing
- Facility elements that might affect cleanliness levels: pressure, airflow uniformity & volume, ventilation effectiveness, temperature, relative humidity
- Facility normal and energy-saving set-back mode
- Facility occupancy & level of activity (as change of shifts)

Main changes in ISO 14644-2

ISO 14644-2:2015 – Monitoring Plan

The monitoring plan shall take into account the output from the risk assessment.

- The plan should reflect the level of air cleanliness required, critical locations and performance attributes of the cleanroom.
- Monitoring plans are **reviewed periodically**; and based on the knowledge gained about the cleanroom or clean zone, the monitoring program is revised

Main changes in ISO 14644-2

The concentration of airborne particles measured under a monitoring plan may be higher than the concentration observed during at-rest classification.

The observed values may fluctuate considerably due to factors such as, but not limited to:

- ✓ number of personnel present,
- ✓ the airflow rate,
- ✓ ventilation effectiveness,
- ✓ the operation of instruments or machinery, and
- ✓ activities in adjacent spaces.

Main changes in ISO 14644-2

For processes that inherently produce particles as part of the process and where these particles are not a threat to the process or product,

It may be appropriate to rely on periodic at-rest classification (at rest), or

operational classification of simulated operations,

rather than monitoring of airborne particles in operation.

Main changes in ISO 14644-2

ISO 14644-2:2015 – Monitoring Plan

- List and justify parameters to be monitored affecting airborne particle concentration:
  - Temperature
  - Humidity
  - cleaning procedures and agents
  - fumigation agents
  - Product materials or process sources for different aerodynamic behaviour (heated surfaces)

Main changes in ISO 14644-2

ISO 14644-2:2015 – Monitoring Plan

- Describe and justify measuring methods (automated vs. manual),
- Identify and justify sample locations (e.g., three dimensions),
- Establish **alarms** and/or alert/action levels
- Explain what will be done if out of limits data found
- **Establish the need and frequency of periodic cleanroom classification** (see periodic classification slide)

Main changes in ISO 14644-2

ISO 14644-2:2015 – Monitoring Plan

- Set the format for recording data
- Relate to trending methods
- Set reporting requirements
- Set the policy and media to be used for record retention
- Set frequency of review of the monitoring plan

Main changes in ISO 14644-2

ISO 14644-2:2015 – Periodic classification

"Periodic classification testing shall be undertaken **annually** in accordance with ISO 14644-1. This frequency can be extended based on risk assessment."

It should be noted that current FDA and EU GMP requirements is for twice a year verification for the aseptic processing room.

Summary- main Changes

ISO 14644-1	ISO 14644-2
• Exclusion of particles > 5 microns from the classification table for ISO Class 5/ Grade A • Number sample points required for classification of a cleanroom • Locating sample points within a cleanroom • Removal of 95% Upper Confidence Limits • Instrument Calibration	• Monitoring Plan • Risk Assessment • Periodic Classification • Alarms

תודה על ההקשבה