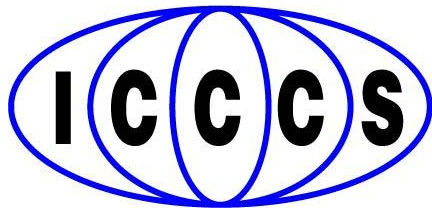


# New ISO 14644-1:2015



**Martin Derks**  
Lighthouse Worldwide Solutions Benelux BV

## New International Standard : ISO 14644-1:2015

1. Title Change
2. Classification Table and (u,M) definitions
3. New Classification Table
4. Impact on GMP table
5. Macro Particle Descriptor
6. Sample Locations
7. Informative Annex A “Cn”
8. The upper confidence level (UCL 95%) evaluation
9. Annex F, Sequential Sampling

# ISO14644-Series

Contaminant	Air Cleanliness by ....	Surface Cleanliness by.....
Particles	<b>ACP: 14644-1</b> Air Cleanliness by Particle concentration	<b>SCP: 14644-9</b> Surface Cleanliness by Particle concentration
Chemicals	<b>ACC: 14644-8</b> Air Cleanliness by Chemical concentration	<b>SCC: 14644-10</b> Surface Cleanliness by Chemical concentration
Nanoparticles	<b>ACN or nACP: 14644-12</b> Air Cleanliness by Nanoscale Particle concentration	
Viables	<b>ACV: 14698-9</b> Air Cleanliness by Viables	<b>SCV: 14698-9</b> Surface Cleanliness by Viables

# ISO 14644-1:2015

## Title Change

<b>ISO 14644-1:1999</b>	<b>ISO 14644-1:2015</b>
Part 1 : Classification of air cleanliness	Part 1 : Classification of air cleanliness by particle concentration
	Impact for users: No change, documentation only

# ISO 14644-1:2015

## Title Change

<b>ISO 14644-2:1999</b>	<b>ISO 14644-2:2015</b>
Part 2 : Specifications for testing and monitoring to prove continued compliance with ISO 14644-1	Part 2 : Monitoring to provide evidence of cleanroom performance by air cleanliness by particles (ACP)
	Impact for users: No change, documentation only

# ISO 14644-1:2015

## Ultra and Micro (u,M) Descriptors

<b>ISO 14644-1:1999</b>	<b>ISO 14644-1:2015</b>
Smaller than 0.1 microns defined as u, larger than 0.5 microns defined as M.	Smaller than 0.1 micron particles will no longer exist in ISO 14644-1. This issue will address in ISO 14644-12 (Air cleanliness by nano particles).
	Impact for users: Classification can be done for smaller particles (<0,1 $\mu$ m) and larger particles using M descriptor

# ISO 14644-1:2015 Class Table

**Maximum concentration limits (particles M<sup>3</sup> of air) for particles equal to and larger than the considered sizes shown below: (a)**

ISO Classification Number(N)	0.1µm	0.2µm	0.3µm	0.5µm	1.0µm	5.0µm
ISO 1	b 10	d <del>2</del>	d	d	d	e
ISO 2	100	24	10	d <del>4</del>	d	e
ISO 3	1,000	237	102	35	d <del>8</del>	e
ISO 4	10,000	2,370	1,020	352	83	e
ISO 5	100,000	23,700	10,200	3,520	832	d,e,f <del>29</del>
ISO 6	1,000,000	237,000	102,000	35,200	8,320	293
ISO 7	c	c	c	352,000	83,200	2,930
ISO 8	c	c	c	3,520,000	832,000	29,300
ISO 9	c	c	c	35,200,000	8,320,000	293,000

**5.0µm should be zero according to ISO/DIS 14644-1.2 Table 1 notes;**

- d) Sampling and statistical limitations for particles in low concentrations make classification inappropriate
- e) ... Greater than 1 micron particles make classification at this particle size inappropriate due to potential particle losses in sampling system
- f) Specify particle size in association with ISO Class 5, the marcoparticle descriptor M may be adapted.

# ISO 14644-1:2015

**Should ISO Class 5 include 5.0 micron as a test size?**

<b>ISO 14644-1:1999</b>	<b>ISO 14644-1:2015</b>
ISO Class 5 ; 5.0 micron : 29 pcs.	No more ISO Class 5 ; 5.0 micron definition.
	Impact on users : Firmware revision. Recipe & reports revision Also different algorithms due to d and e. Will make a difference between GMP and ISO reports.



# GMP ANNEX 1

## MANUFACTURE OF STERILE MEDICINAL PRODUCTS

### Clean room and clean air device classification

The maximum permitted airborne particle concentration for each grade is given in the following table.

Grade	Maximum permitted number of particles per m <sup>3</sup> equal to or greater than the tabulated size			
	At Rest		Operational	
	0.5µm	5.0µm	0.5µm	5.0µm
A	3,520	20	3,520	20
B	3,520	29	352,000	2,900
C	352,000	2,900	3,520,000	29,000
D	3,520,000	29,000	Not Defined	Not Defined

**Class limit of 20 parts ≥ 5.0 micron outside scope**

**Class limit of 29 parts ≥ 5.0 micron outside scope**

# Using the macro-particle descriptor for 5 micron particles

- GMP Should use the macro-particle concept for  
Grade A                      20 particles/m<sup>3</sup> @ ≥ 5.0 micron  
Grade B “at rest”        29 particles/m<sup>3</sup> @ ≥ 5.0 micron

- We use this terminology  
ISO M (20; ≥ 5.0); LSAPC

M=  
Macroparticles

20 =  
Class limit  
from GMP

Considered  
particle  
size

LSAPC = Light  
scattering  
airborne  
particle counter

# Using the macro-particle descriptor for 5 micron particles

- **Grade A**

ISO 5; at rest, operational;  $\geq 0.5$

ISO M (20;  $\geq 5.0$ ); at rest, operational; LSAPC

- **Grade B**

ISO 5; at rest;  $\geq 0.5$ , and M (29;  $\geq 5.0$ ); at rest, LSAPC.

ISO 7; operational;  $\geq 0.5, 5.0$  .

## Using the macro-particle; other examples:

- 2500 particles/m<sup>3</sup> for 10μm

ISO M (2500; ≥ 10.0); at rest, time-of-flight aerosol particle counter

- 1000 particles/m<sup>3</sup> for range 10μm to 20μm

ISO M (1000; 10 to 5.0μm); at rest, microscope.

# ISO 14644-1:2015

## Informative Annex A (Cn Definition)

ISO 14644-1:1999	ISO 14644-1:2015
$C_n = 10^N X \left[ \frac{0,1}{D} \right]^{2,08}$	<p>Table 1 only, no Cn formulation                      No more decimal classes. (4.8 etc.)                      Annex F for intermediate decimal cleanliness classes (3.5, 4.5, 5.5 etc.)</p>
	<p>Impact on users :                      Not frequently used; change reporting</p>

# ISO 14644-1:2015 Decimal Class Table (only .5)

Maximum concentration limits (particles M<sup>3</sup> of air) for particles equal to and larger than the considered sizes shown below: (a)

ISO Classification Number(N)	0.1µm	0.2µm	0.3µm	0.5µm	1.0µm	5.0µm
ISO 1,5	b[32]	d	d	d	d	e
ISO 2,5	316	b[75]	b[32]	d	d	e
ISO 3,5	3.160	748	322	d	d	e
ISO 4,5	31.600	7.480	3220	1.110	263	e
ISO 5,5	316.000	74.800	32.200	11.100	2.630	e
ISO 6,5	3.160.000	748.000	322.000	111.000	26.300	924
ISO 7,5	c	c	c	1.111.000	263.000	9.240
ISO 8,5	c	c	c	11.100.000	2.630.000	92.400

Intermediate particle sizes:

$$C_n = 10^N X \left[ \frac{K}{D} \right]^{2,08}$$

*e.g. ≥0,4µm*

# ISO 14644-1:2015

## Sample Numbers and Locations

ISO 14644-1:1999	ISO 14644-1:2015
<p>Square-root Method for sample numbers. <math>N = \sqrt{A}</math></p> <p>Grid for sample locations</p>	<p>Table A.1. (Fixed numbers)</p>
	<p>Impact for users: Adjustment for SOP's</p>

## Min. req. Sample locations

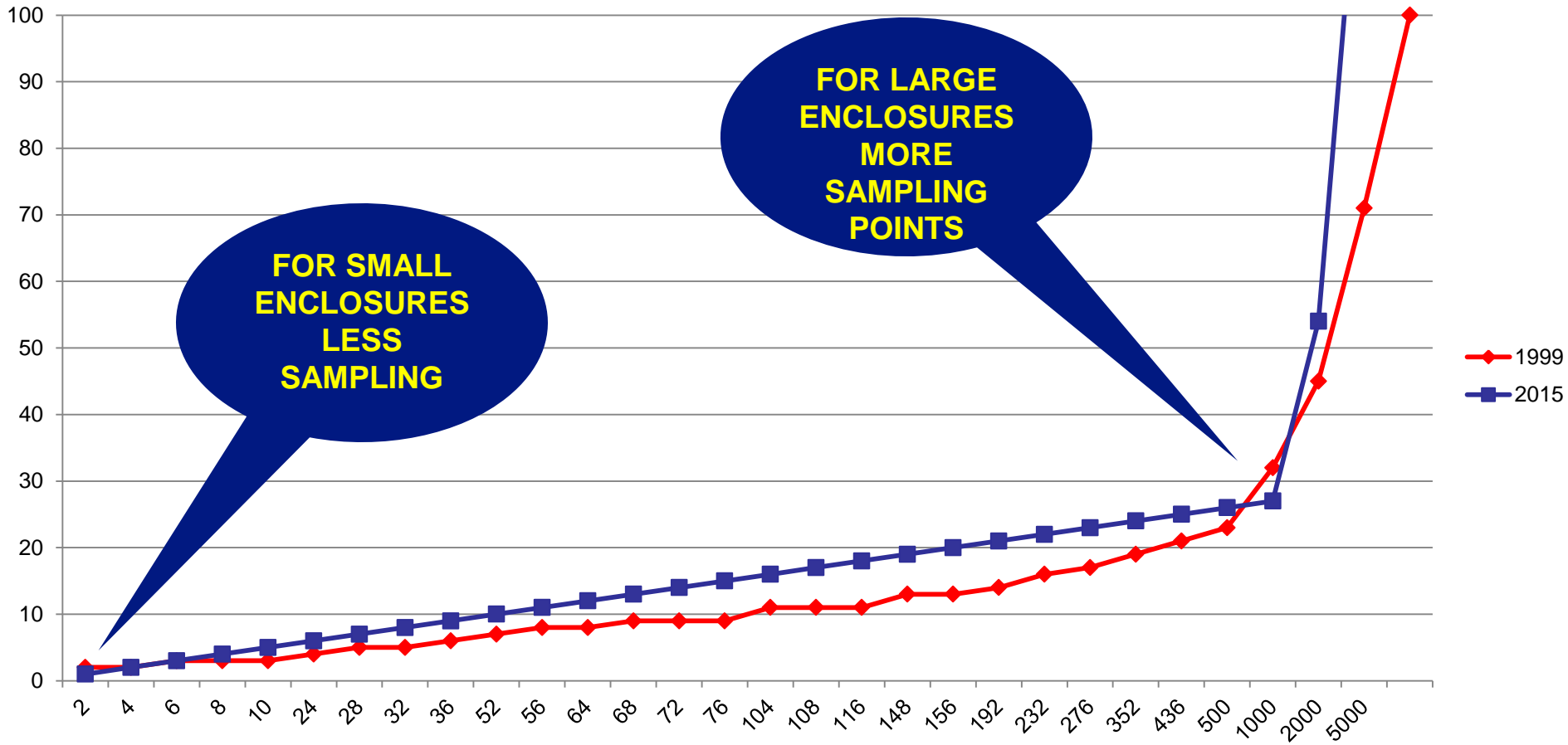
Number and selection of locations:

- ISO 14644-1:1999
  - $\sqrt{(\text{surface area})}$
- ISO 14644-1:2015
  - Acc. To Table
  - No Random selection
  - No UCL calculations
  - Evenly divided over cleanroom.
  - $> 1000 \text{ mtr } N = 27 \left[ \frac{A}{1000} \right]$

Area of cleanroom (m2) Less than or equal to	Min number of sample locations to be tested NL
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
72	14
76	15
104	16
108	17
116	18
148	19
156	20
192	21
232	22
276	23
352	24
436	25
500	26
1000	27
>1000	Equation A.1



# Minimum required Sample locations



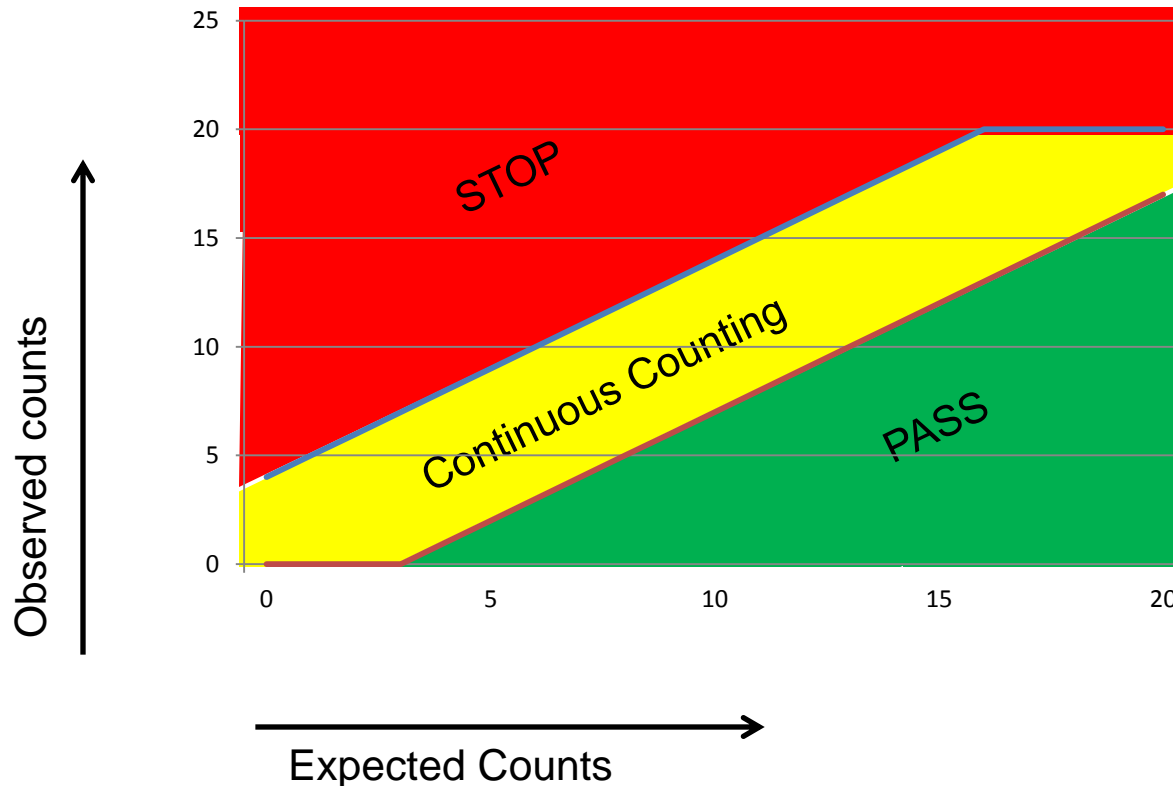
# ISO 14644-1:2015

## UCL 95%

<b>ISO 14644-1:1999</b>	<b>ISO 14644-1:2015</b>
1<x<9 sample points, UCL 95% should be calculated	Removed completely.
	Impact on users : Particle Counter Firmware revision. Reports, Recipes Remove UCL 95%

# Sequential sampling

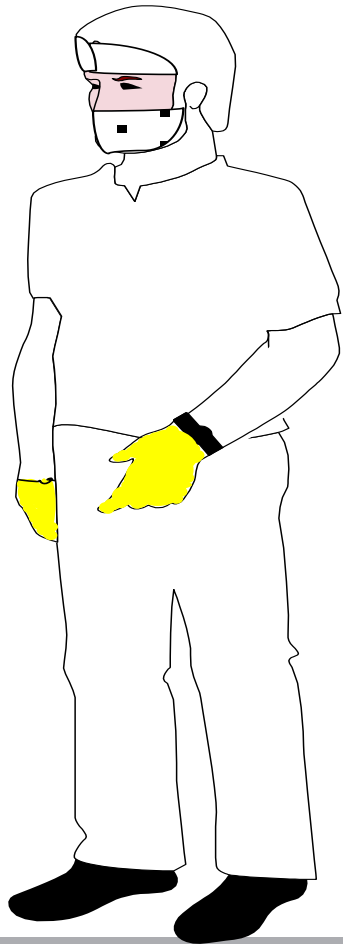
$$\text{Expected Counts} = \frac{Q \times t \times C_{n,m}}{1000}$$



# ISO 14644-1:2015

## ISO 21501-4 Attribution

<b>ISO 14644-1:1999</b>	<b>ISO 14644-1:2015</b>
«Latest standard available...»	Calibration method clearly states that ISO21501-4 should perform for particle counter calibration.
	Impact on users : All particle counters should compliant No more «ISO9001» certs.



*Vragen?*

*Bedankt voor uw aandacht*