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Cleanrooms and associated controlled environments —

Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration

Salles propres et environnements maîtrisés apparentés —

Partie 2: Surveillance du maintien des performances de la salle propre pour la propreté particulaire de l'air

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT) see the following URL: Foreword - Supplementary information

The committee responsible for this document is ISO/TC 209, *Cleanrooms and associated controlled environments*.

This second edition cancels and replaces the first edition (ISO 14644-2:2000), which has been technically revised throughout.

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*

Attention is also drawn to ISO 14698, *Cleanrooms and associated controlled environments — Bio-contamination control*:

— *Part 1: General principles and methods*

— *Part 2: Evaluation and interpretation of bio-contamination data*

Introduction

This revision of ISO 14644-2 emphasizes the need to consider a monitoring strategy in addition to the initial or periodic execution of the classification of a cleanroom or clean zone in accordance with ISO 14644-1:2015, 5.1. The monitoring activity provides a continuing flow of data over time, thereby providing a more detailed view of the performance of the installation.

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.

ISO 14644-2 specifies the requirements of a monitoring plan, based on risk assessment of the intended use. The data obtained provide evidence of cleanroom or clean zone performance related to air cleanliness by particle concentration.

In some circumstances, relevant regulatory agencies may impose supplementary policies, requirements or restrictions. In such situations, appropriate adaptations of the monitoring procedures may be required. After a monitoring plan is initially established and implemented, it may be necessary to revise the plan when significant changes are made to the installation or process requirements. It is also prudent to conduct periodic reviews of a monitoring plan based on data obtained and experience in use.

Cleanrooms and associated controlled environments —

Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration

1 Scope

This part of ISO 14644 specifies minimum requirements for a monitoring plan for cleanroom or clean zone performance related to air cleanliness by particle concentration, based upon parameters that measure or affect airborne particle concentration.

This part of ISO 14644 does not address condition monitoring of aspects such as vibration or general maintenance of the engineering systems. It does not provide for monitoring of particle populations that are outside the specified lower threshold particle-size range 0,1 µm to 5 µm. Concentrations of ultrafine particles (particles smaller than 0,1µm) will be addressed in a separate standard.

2 Normative references

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 14644-1:2015, *Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 14644-1 and the following apply:

3.1
test
procedure undertaken in accordance with a defined method to determine the performance of an installation or an element thereof

3.2
monitoring
observations made by measurement in accordance with a defined method and plan to provide evidence of the performance of an installation

Note 1 to entry: Monitoring may be continuous, sequential or periodic; and if periodic, the frequency shall be specified.

Note 2 to entry: This information may be used to detect trends in operational state and to provide process support.

3.3
action level
level of a parameter set by the user which, when exceeded, requires immediate intervention, including investigation of cause, and corrective action

3.4
alert level
level of a parameter set by the user giving early warning of a drift from normal conditions, which, when exceeded, should result in increased attention or corrective action

4 Creating, implementing and maintaining a monitoring plan

4.1 Principle

In order to gain assurance that a cleanroom or clean zone is performing adequately by delivering the required control of air cleanliness by particle concentration, a monitoring plan shall be created, implemented and maintained.

A monitoring plan shall take into account the level of air cleanliness required, critical locations and performance attributes of the cleanroom or clean zone that affect the performance of the installation. The following steps shall be included in the creation, implementation and maintenance of the monitoring plan:

— use appropriate risk assessment tools to understand, evaluate and document the risk of adverse contamination events;

— develop a written monitoring plan;

— review and approve the plan;

— implement the plan by performing the monitoring;

— analyse the data derived from the monitoring activity, undertake trend analysis where appropriate and report performance;

— implement and document actions or corrective actions required;

— undertake periodic review of the monitoring plan.

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

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, or operational classification of simulated operations, rather than monitoring of airborne particles in operation. Other performance and cleanliness attributes may still be required to be monitored.

4.2 Risk assessment

Risk assessment is a systematic process of identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards.

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 by particle concentration of the cleanroom or clean zone, and

— determine the monitoring requirements to provide evidence of performance.

For guidance on what to consider when undertaking a risk assessment, see informative Annex A.

4.3 Monitoring plan

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

When developing the monitoring plan, the factors described in 4.3.2 to 4.3.13 shall be included as a minimum.

4.3.2 Listing and justification of all the parameters to be monitored, including those that may affect the airborne particle concentration.

4.3.3 Description and justification of measurement methods. For further guidance on considerations when developing a monitoring plan, see informative Annex A.

4.3.4 Accuracy, maintenance and calibration of monitoring instrumentation.

4.3.5 Identification and justification of selected monitoring locations. Monitoring locations shall be defined in three dimensions.

4.3.6 Identification and justification of monitoring acceptance criteria or limits, including establishment of a single alarm level, or a dual alarm approach of alert and action levels. The minimum requirement is that a single alarm action level is established. Additionally, an alarm alert level can be established to provide early warning of performance deviation. For further guidance on setting alert and action levels, see informative Annex B.

4.3.7 Specification of the response required should the data fall outside the specified limits.

4.3.8 The need for and frequency of periodic cleanroom or clean zone air cleanliness classification by particle concentration in accordance with ISO 14644-1:2015, 5.1.

4.3.9 The format for recording data.

4.3.10 The methods, including statistical methods to be used for data trending or other appropriate analysis.

4.3.11 The reporting requirements.

4.3.12 The policy and media to be used for record retention.

4.3.13 The frequency of review of the monitoring plan.

NOTE Monitoring plans are reviewed periodically; and based on the knowledge gained about the cleanroom or clean zone, the monitoring programme is revised.

4.4 Calibration

Instrumentation used for monitoring shall be adequate to perform the monitoring operations required, shall have a valid calibration certificate, and shall meet current accepted practices for the frequency and method of calibration.

In particular for airborne particle counters, the frequency and method of calibration should be based upon current accepted practice as specified in ISO 21501-4.

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 monitoring plan.

4.5 Review and approval

The completed plan shall be reviewed and approved.

4.6 Response to a deviation during monitoring

If monitoring results exceed the specified limit(s), an investigation shall be conducted to determine cause, and remedial action taken as required.

If the remedial action requires significant changes to the installation and/or its operation, then the classification test according to ISO 14644-1 shall be undertaken. The monitoring plan shall also be reviewed as a result of the changes to the installation and/or its operation.

When the desired classification has been achieved, monitoring may be resumed.

5 Periodic classification of air cleanliness by particle concentration

Periodic classification testing shall be undertaken annually in accordance with ISO 14644-1. This frequency can be extended based on risk assessment, the extent of the monitoring system, and data that are consistently in compliance with acceptance limits or levels defined in the monitoring plan.

NOTE ISO 14644-3 specifies ancillary tests related to other aspects of cleanroom performance such as pressure difference, airflow, etc.

Annex A
(informative)

Matters to consider when developing a monitoring plan

A.1 Risk assessment considerations

A.1.1 Selection of an appropriate risk assessment tool

Risk assessment can be undertaken using a number of tools – separately or in combination – including but not limited to

— HACCP,

— FMEA / FMECA,

— PHA,

— FTA, and

— HAZOP.

A.1.2 Definition of required performance and operating conditions that may need to be monitored

These can be factors such as

— understanding the contamination sources and their impact on the activity in the cleanroom or clean zone at critical locations or at locations representative of the general air cleanliness in a cleanroom or clean zone,

— performance of the installation that might affect the cleanliness levels such as pressure differential, airflow uniformity, airflow volume, ventilation effectiveness, temperature, relative humidity,

— normal and energy-saving set-back mode,

— at-rest or operational states, and

— occupancy and level of activity, such as change of shift.

A.2 General considerations

A.2.1 The general matters described in A.2.2 to A.2.21 should be considered when developing a monitoring plan.

A.2.2 The measurement technique, including the selection of manual and/or automated monitoring.

A.2.3 The resolution, accuracy and calibration requirements of the measurement system including, in the case of airborne particle counters, the efficiency and limitations of the collection system.

A.2.4 The location of monitoring system components, including requirements for access for maintenance and calibration.

A.2.5 Instrument or sample probe location, configuration and orientation.

A.2.6 Identification of frequency of measurement or sampling in order to detect deviation events.

A.2.7 Consideration of issues that may influence the monitoring system or the results obtained, such as (but not limited to) temperature, humidity, cleaning procedures and agents, fumigation agents, product materials or process hazards and sources of potential convection currents in the air due to heated surfaces.

A.2.8 Consideration of any potential adverse impact of the sampling system on the process or the process environment (e.g. possible effects of the extraction of the air-sample volume required by a particle counter on small enclosed environments).

A.2.9 The results of any airflow visualization studies such as "smoke studies," computer airflow modelling simulations or other studies.

A.2.10 Understanding the ventilation effectiveness in the cleanroom or clean zone, as might be affected by rate of air exchanges, recovery or clean-up time studies, or any other method to understand the potential rate of removal of airborne particles.

A.2.11 Extent and/or frequency of cleaning or maintenance procedures and their impact on airborne particle levels, both during execution and immediately after completion of the procedure.

A.2.12 Consideration of process-related events that may affect environmental conditions at monitoring locations. Such events may include (but are not limited to) dismantling, cleaning and reassembly of equipment, whether as part of the process cycle or as an element of maintenance work.

NOTE It may be useful to include within the monitoring plan provisions for monitoring the recovery time at the conclusion of such refitting, prior to resuming normal operations.

A.2.13 Typical positions and movements of personnel during the critical operational periods.

A.2.14 Expectations for the number of personnel active in the cleanroom or clean zone, the nature of their occupation and the duration of their activities.

A.2.15 Assessment of the impact of equipment-generated changes to airflow patterns.

A.2.16 Assessment of the potential for equipment-generated particle sources. Examples include particles generated from abrasion of surfaces on moving conveyor systems, and processes such as sealing of glass ampoules and radio frequency (RF) welding of tubing.

A.2.17 Data logging and data management, including data integrity, storage and retrieval

NOTE In some industries the storage and integrity of data are specifically regulated.

A.2.18 Establishment of suitable techniques for the evaluation of raw data, assessment of trends, and production of reports.

A.2.19 Definition of acceptance criteria and establishment of a single alarm level, or a dual approach of alert and action levels.

A.2.20 Requirements for commissioning and testing of the monitoring system(s).

A.2.21 Requirements for maintenance of the monitoring system(s).

A.3 Pressure differential monitoring

A.3.1 The additional aspects described in A.3.2 to A.3.5 should be considered for specifying monitoring systems for differential pressures in cleanrooms or clean zones.

A.3.2 The method of minimising or managing fluctuations caused by disturbances such as door openings or intermittent operation of local exhaust systems. A common method is the introduction of time delays on alarms.

A.3.3 Selection of a pressure-measurement reference principle (measurement of differential pressure between rooms or spaces, or measurement of differential against a common reference pressure).

A.3.4 Establishment of alert and action levels that are sensitive to normal pressure fluctuations due to factors such as wind effects on buildings, the opening and closing of doors and other factors.

A.3.5 The pressure differential may be monitored by periodic observation or by automated instrumentation.

A.4 Airborne particle monitoring system

A.4.1 The additional aspects described in A.4.2 to A.4.6 should be considered for specifying real-time airborne particle counting systems.

A.4.2 The configuration of the system based on evaluating the following system attributes:

— airborne particle collection efficiency;

— suitability to monitor the selected particle size(s);

— accessibility for maintenance, calibration, and repair.

NOTE 1 These considerations will influence the choice between using multiple local “point of use” particle counters or using a single particle counter with a multiplexing manifold and long sample transport tubes.

NOTE 2 The use of long sample transport tubes as required by multiplexing manifold systems is inappropriate for monitoring particle sizes ≥ 5 µm.

A.4.3 Air sample flow rate and volume.

A.4.4 The frequency and duration of the collection of each air sample (determined by the sampling rate).

A.4.5 The sample probe configuration and orientation with respect to airflow (e.g. isokinetic or an-isokinetic).

NOTE It may not be appropriate to locate a sample probe directly under a supply air terminal High-Efficiency Particulate Air (HEPA) filter in a non-unidirectional airflow configuration because such a location may not be representative of the cleanroom or clean zone, and may prevent detection of contamination events in operation.

A.4.6 Potential adverse impact of the sampling system on the process or the process environment (e.g. possible effects of the rate of the extraction of the sample volume in small volume environments).

A.5 Airflow velocity and volume monitoring

A.5.1 The additional aspects described in A.5.2 to A.5.3 should be considered for specifying airflow velocity or air volume monitoring systems.

A.5.2 The selected airflow velocity or volume measurement technique.

A.5.3 The location of the measurement device so that the measurement is representative of the system being monitored.

NOTE It may be necessary to evaluate locations to prove measurements are representative and not adversely influenced by airflow turbulence or uneven flow in ducts or other factors.

Annex B
(informative)

Considerations for setting alert and action levels

B.1 General basis for setting alert and action levels

The establishment of alert- and action-level alarms requires careful consideration to ensure they provide an effective basis for initiating a response, such as further investigation or increased observation (known as an "alert level"), and trigger a remedial action response (designated as an "action level"). The following should be considered:

— the intent and purpose of monitoring;

— the importance and/or criticality of the monitored parameters;

— the selection of a single alarm action level or dual alarm alert and action levels;

— the risk from failing to react to the "alert" or "action" due to high frequency of alarms. This may occur from setting inappropriate alarm levels and may result in personnel not acting upon or muting alarms;

— how normal acceptable fluctuations in monitored parameters are managed; for example, the rationale for time delays and the algorithms for rate of change prediction systems;

— frequency of sampling or measurement to enable assessment of the rate at which the next data point will be acquired;

— when responding to an "alert," the ability to respond, the nature of the response and the time allowed for the response before it is elevated to an "action."

B.2 Setting alert and action levels for pressure differential monitoring

B.2.1 Establishing the normal operational range for pressure differentials

In order to set alert and action levels for pressure differentials, it is necessary to establish the normal operating range, including, for example, fluctuations due to doors opening and equipment interactions. Deviations from this normal operating range can then be established in terms of either solely a value deviation or a value and time of deviation.

The initial observations should be repeated periodically and after maintenance or modification of a cleanroom or clean zone due to variations in performance and ageing of components of the installation.

The approach given in B.2.1.1 and B.2.1.2 should be adopted to explore and document pressure fluctuations.

B.2.1.1 The impact of operating airlock doors

Air locks are designed to help maintain pressure differentials as personnel or materials move from one cleanroom or clean zone to another. Air locks are designed or operated so that one opposing door set is always closed. However, unless the doors are equipped with inflatable seals, the leakage through the airlock is usually greater when one of the opposing door sets is open than when they are both closed.

It is necessary to test and document these normal variations to properly set alert and action levels for pressure alarms. Follow this procedure:

— close all doors and pass-through hatches, define the operational status of any equipment, and observe the steady-state pressure differentials between the selected rooms or zones noting the small, normal fluctuations that will occur due to wind and other dynamic effects;

— for each airlock, pass-through hatch or transfer chamber, open all the doors, one set of opposing doors at a time, and note room- or zone-pressure variation. Close the doors and confirm that the pressure differentials return to their original values;

— leakage paths, such as those around doors, should be evaluated as part of a cleanroom design to ensure adequate allowance is made in the air balance for such leakages.

B.2.1.2 The impact of process equipment

Some process equipment have a small and acceptable effect on room or zone pressure differentials due to small changes in the air lost from pressurized spaces via the equipment when functioning in different operational states. Follow this procedure:

— close all doors and pass-through hatches, set the equipment in a defined operational state, and observe the steady-state pressure differentials between the selected rooms or zones noting the small, normal fluctuations that occur due to wind and other dynamic effects;

— repeat the test for each of the different operational states of the equipment. For each state, observe the steady-state pressure differentials between the selected rooms or zones noting the small normal fluctuations that occur due to wind and other dynamic effects.

B.2.2 Setting alert and action levels

B.2.2.1 After observing and recording the normal operating ranges, it is recommended that a pressure setting for the warning pressure measurement device be selected a few Pascal below the lowest pressure observation for a positive-pressure configuration, or a few Pascal above in a negative-pressure configuration (guidance value 2 Pa to 3 Pa).

B.2.2.2 It is often necessary to delay the alert or action alarm to allow for normal activity in the cleanroom, such as the opening of doors to permit entry and exit of personnel. Careful observation of the duration of typical or expected normal deviation is necessary to determine appropriate time delay. Deviations that extend beyond the normal durations should activate warnings.

B.2.2.3 Managing excessive pressure fluctuations or leakage by simply increasing the pressure differentials is not recommended because air leakage will be increased further with associated inefficiencies in the performance of the air-conditioning or ventilation system.

B.2.2.4 In regulated industries there is an expectation that root causes of problems will be identified and rectified rather than being accommodated by changes in operational limits. Failure to identify the root cause may lead to adverse regulatory action.

B.2.3 Pressure differential instrumentation

B.2.3.1 When pressure switches are used, ensure that the action of the pressure switch is repeatable and that any switching hysteresis is accounted for and accommodated by the setting of the alert or action level.

B.2.3.2 To simplify calibration and avoid the need to remove instruments from the installation, especially when instrumentation is mounted in areas that are difficult to access, the instruments should be fitted with test ports and a method to isolate the instruments from the pressure source to enable the zero and span to be determined.

B.3 Setting alert and action levels for airborne particle counts

B.3.1 General guidance

B.3.1.1 The objective of particle concentration count monitoring in an operational cleanroom or clean zone is to provide evidence that the required level of cleanliness is achieved at critical control points. Risk assessment and evaluation of data from formal cleanroom or clean zone classification in accordance with ISO 14644-1 should be used to determine the monitoring locations (critical control points). The alert and action levels identified should provide effective information to allow management of performance changes and identification of deviations from defined acceptance criteria.

NOTE Statistical process control principles can be used to set alert and action levels based on analysis of historical data.

B.3.1.2 It is essential to establish appropriate methods to annunciate or indicate when the particle count values reach alert or action levels.

B.3.1.3 When setting alert and action levels, it is important to be sensitive to the high variability of airborne particle concentrations with time and at different locations. In particular, special care shall be taken when considering alert and action levels for cleanliness classes ISO Class 5 and cleaner with low concentrations of particles. In these circumstances, the occurrence of "nuisance alarms" due to false counts and/or natural variability of particle concentration is more likely and should be avoided by careful selection of alert and action levels. Frequent "nuisance" alarms should be avoided as they can lead to alarms being ignored by users.

B.3.1.4 The consistency of the physical sampling position and the orientation of the sample probe can have a marked effect on the particle concentration measured. This is especially true when there is a need to compare the values from one sample period to the next. It is important that the position of the sample does not change substantially without due consideration of the impact on trending history and alert and action levels.

B.3.2 Establishing normal operating range for particle counts

B.3.2.1 Initially measure and record the particle concentration at the designated critical control points over a significant period of time, in both the "at rest" and "operational" occupancy states. The intended sampling time and sample size should be used. From this set of data, the expected normal performance of the cleanroom or clean zone can be determined and become the basis for establishment of the alert and action levels. It is anticipated that these normal values will be below the ISO cleanliness class limit or action level.

B.3.2.2 It may be necessary to conduct a subsequent period of observation when a major change occurs to the design or operation of the installation.

B.3.2.3 Particle count data have some unique characteristics that should be understood. The following are important:

a) the particle concentration baseline in a space is highly dependent on the level of activity, the volume of the cleanroom or clean zone, and the ventilation mechanism and effectiveness;

b) it is good practice to investigate particle count readings that are consistently lower than the expected norms because this may be an indication of the malfunction of the particle counter, air sample acquisition system or data-logging apparatus;

c) the acceptable range of particle concentrations for the "at rest" state may be significantly lower than the "operational" state in non-unidirectional airflow systems;

d) warning values may need to be different for different sample points within the same room or zone;