INTERNATIONAL STANDARD

ISO 14698-2

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Cleanrooms and associated controlled environments — Biocontamination control —

Part 2: Evaluation and interpretation of biocontamination data

Salles propres et environnements maîtrisés apparentés — Maîtrise de la biocontamination —

Partie 2: Évaluation et interprétation des données de biocontamination

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this part of ISO 14698 may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

International Standard ISO 14698-2 was prepared by Technical Committee ISO/TC 209, *Cleanrooms and associated controlled environments*.

ISO 14698 consists of the following parts, under the general title *Cleanrooms and associated controlled environments — Biocontamination control*:

— *Part 1: General principles and methods*

— *Part 2: Evaluation and interpretation of biocontamination data*

Introduction

This part of ISO 14698 presents a framework for the evaluation of biocontamination data collected following the principles and methods given in ISO 14698-1. It may also be applied to biocontamination data collected by other systems.

Cleanrooms and associated controlled environments — Biocontamination control —

Part 2: Evaluation and interpretation of biocontamination data

1 Scope

This part of ISO 14698 gives guidance on methods for the evaluation of microbiological data and the estimation of results obtained from sampling for viable particles in risk zones for biocontamination control. It should be used, where appropriate, in conjunction with ISO 14698-1.

2 Normative references

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

ISO 14698-1:2003, *Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1
action level
microbiological level set by the user in the context of controlled environments, which, when exceeded, requires immediate intervention, including investigation of cause, and corrective action

3.2
alert level
microbiological level set by the user for controlled environments, giving early warning of a potential drift from normal conditions

NOTE When alert levels are exceeded, this should result in increased attention to the process.

3.3
audit trail
chain of related documents, or entries within records, that allows related information to be traced

3.4
biocontamination
contamination of materials, devices, individuals, surfaces, liquids, gases or air with viable particles

3.5
cleanroom
room in which the concentration of airborne particles is controlled, and which is constructed and used in a manner to minimize the introduction, generation, and retention of particles inside the room, and in which other relevant parameters, e.g. temperature, humidity and pressure, are controlled as necessary

[ISO 14644-1:1999, 2.1.1] [1]

3.6
data stratification
regrouping of data so that important trends and deviations can be more easily seen and understood

3.7
estimate
value of an estimator obtained as a result of an estimation

[ISO 3534-1:1993, 2.51] [2]

3.8
estimation
operation of assigning, from the observations in a sample, numerical values to the parameters of a distribution chosen as the statistical model for the population from which this sample is taken

[ISO 3534-1:1993, 2.49] [2]

3.9
estimator
statistic used to estimate a population parameter

[ISO 3534-1:1993, 2.50] [2]

3.10
hazard
biological, chemical or physical element or factor that adversely affects individuals, the environment, process or product

3.11
risk
combination of the probability of the occurrence of harm and the severity of that harm

[ISO/IEC Guide 51:1999, 3.2] [8]

3.12
risk zone
defined and delimited space where individuals, products or materials (or any combination of the above) are particularly vulnerable to biocontamination

3.13
target level
defined microbiological level set by the user, for its own purpose

3.14
validation
confirmation, through the provision of objective evidence, that the requirements for a specific intended use or application have been fulfilled

[ISO 9000:2000, 3.8.5] [3]

3.15
viable particle
particle that consists of, or supports, one or more live microorganisms

3.16
viable unit
VU
one or more viable particles that are enumerated as a single unit

NOTE When VU are enumerated as colonies on agar media, it is common usage to name them colony-forming units (CFU).

4 Evaluation and interpretation of biocontamination data

4.1 General

Information on the setting of action, alert and, where appropriate, target levels, the validation of counting methods and the collection of biocontamination data are discussed in ISO 14698-1. This part of ISO 14698 discusses the evaluation and interpretation of the data collected.

Management of microbiological results from risk zones should take the following factors into account:

— types of result to be collected;

— necessary information;

— methods to process the collected results (e.g. statistical procedures, correlation analysis, artificial intelligence, etc.);

— grouping of results to focus on important trends and deviations, i.e. data stratification;

— method by which the results will be expressed (e.g. qualitatively, quantitatively, graphically, numerically) and the units of measurement that will be used;

— robustness of, and potential problems posed by, the analytical methods;

— trend analysis;

— control charting;

— estimation, interpretation and reporting of results.

It is recommended that the evaluation of results be performed in two stages: during the initial monitoring (set-up procedure) phase and during the routine monitoring phase.

4.2 Estimation and evaluation of data from the initial monitoring phase (set-up procedure — see Figure 1)

4.2.1 Significance of biocontamination

To obtain reliable estimates of biocontamination gathered according to ISO 14698-1, it is necessary to consider the following variables:

— sampling-adequate number and homogeneity of the sample material and accuracy of dilution of the samples, if appropriate;

— composition of the viable particle spectrum involved; its variability with time and the effect of stress and injury on survival and recovery;

— results originating from different sampling sites in risk zones and other controlled environments;

— culturing technique and the methodology of counting;

— selection of method of analysis and relationship between direct and indirect testing.

4.2.2 Corrective action

To maintain control over the performance of the testing laboratory, it is very important to identify and eliminate the cause of any errors that may occur. Prompt investigation of out-of-specification results should include attention to the possibility of testing error.

The investigation should include:

— a standard method for highlighting abnormal results;

— elimination of gross or systematic errors;

— evaluation of change;

— establishment of the recovery efficiency of the revised method;

— verification of equipment;

— justification and documentation;

— clear rules to decide how the final result is derived when an analysis has been repeated.

4.2.3 Records

All regular and periodical checks of methods, instruments and internal audits, as well as records of original observations, calculations, derived data and final reports should be appropriately filed and retained. It is essential that the records include the identity of personnel involved in sampling, preparation, testing, evaluation and reporting. It should be possible to conduct an audit trail to show the details of how and when any results have been changed. Records of signatures, initials or signs should be maintained and updated as appropriate. Reports should be distributed as required. This may include mail, facsimile transmission and electronic data transfer.

It is essential that appropriate protection of data and records, including those held in the computer, be provided.

1	**Establish sampling points and sampling plan — Identification of data to be collected** (as described in ISO 14698-1)
	• establish data collection parameters • establish sampling plan • establish/prepare data collection/recording sheets • set preliminary limits
	↓
2	**Preliminary measurement phase** (as described in ISO 14698-1)
	• determine the presence of biocontamination • select methods • conduct sampling and microbiological examinations
	↓
3	**Analysis and monitoring of data**
	• tabulate data, e.g. in evaluation table/matrix • stratify (sort/steamline) preliminary data • express results • apply statistical evaluation procedures with the determination of precision and accuracy • establish control charts
	↓
4	**Data evaluation**
	• evaluate initial limits at control points • assign target/alert/action levels from preliminary measurements • consider out-of-specification results
	↓
5	**Standardization and validation**
	• sampling, measuring methods • electronic data processing • personnel training
	↓
6	**Data storage/Documentation/Archive**

Figure 1 — Estimation and evaluation of data from initial monitoring phase