



BSI Standards Publication

**Nanotechnologies — Aerosol generation for
air exposure studies of nano-objects and their
aggregates and agglomerates (NOAA)**

National foreword

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**Nanotechnologies — Aerosol
generation for air exposure studies of
nano-objects and their aggregates and
agglomerates (NOAA)**

*Nanotechnologies — Génération d'aérosols pour réaliser des
études d'exposition à l'air des nano-objets et de leurs agrégats et
agglomérats (NOAA)*



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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.

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 voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 229, *Nanotechnologies*.

Introduction

Inhalation is a primary route of exposure to aerosolized nano-objects and their aggregates and agglomerates (NOAA). The NOAAs include nano-objects with one, two or three external dimensions in the nanoscale from approximately 1 nm to 100 nm, which might be spheres, fibres, tubes and others as primary structures. NOAAs can consist of individual primary structures in the nanoscale and aggregated or agglomerated structures, including those sizes larger than 100 nm. To evaluate the inhalation toxicity of NOAA, it is important to consider certain parameters that make the toxicity testing relevant to human exposure. The three critical aspects to consider when designing and conducting nanomaterial inhalation toxicity study are

- a) uniform and reproducible nano-object aerosol generation that is relevant to realistic exposures;
- b) thorough characterization of nanomaterials throughout the duration of testing including starting and generated materials, and
- c) use of occupational exposure limits (OEL) and reference concentrations (RfC) (as derived from existing studies and/or real-time exposure monitoring data) for dosimetry.

Therefore, to conduct *in vitro* and *in vivo* NOAA, it is important to choose an appropriate NOAA aerosol generator and use online and off-line techniques for nano-object characterization.

Aerosol generation techniques are well established and have been used in laboratory studies, inhalation therapy and industry for many years. A number of aerosol generation techniques are routinely used for other materials that can be adapted for nano-object inhalation toxicity studies. In principle, aerosol generation involves application of some form of energy to the material to reduce its size or to form small particles that are dispersed in a gas stream.

This document provides the status of nano-object aerosol generators. This document further discusses the advantages and limitations of the respective nano-object generators, which can aid in choosing the appropriate generator when conducting the nano-object inhalation toxicity study. No matter what generation system is used for toxicity study, the generated atmospheres should be thoroughly characterized in order to allow for comparison to occupational exposure atmospheres so that a valid risk assessment/occupational exposure limit (OEL) can be developed. Therefore, this document will also provide nano-object aerosol size information generated from respective generators along with the proper nano-object characterization methods. This document complements the work of the Organization for Economic Cooperation and Development (OECD) Working Party on Manufactured Nanomaterial (WPMN) and other related framework documents. Recommendations and guidelines to assist investigators in making appropriate choices of an aerosol generator for their target NOAAs to be tested are presented in this document.

Nanotechnologies — Aerosol generation for air exposure studies of nano-objects and their aggregates and agglomerates (NOAA)

1 Scope

This document describes methods for producing aerosols of nano-objects and their aggregates and agglomerates (NOAA) for *in vivo* and *in vitro* air exposure studies. The purpose of this document is to aid in selecting an appropriate aerosol generator to fulfil a proposed toxicology study design. This document describes characteristics of aerosol generation methods, including their advantages and limitations. This document does not provide guidance for aerosolization of specific nano-objects.

2 Normative references

The following documents are referred to in the text in such a way that none or all of their content constitutes requirements 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/TS 80004-1, *Nanotechnologies — Vocabulary — Part 1: Core terms*

ISO/TS 80004-2, *Nanotechnologies — Vocabulary — Part 2: Nano-objects*

ISO/TS 80004-4, *Nanotechnologies — Vocabulary — Part 4: Nanostructured materials*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO/TS 80004-1, ISO/TS 80004-2, and ISO/TS 80004-4 and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

- IEC Electropedia: available at <http://www.electropedia.org/>
- ISO Online browsing platform: available at <http://www.iso.org/obp>

3.1

aerodynamic diameter

diameter of a spherical particle with a density of 1 000 kg/m³ that has the same settling velocity as the *particle* (3.29) under consideration

Note 1 to entry: Aerodynamic diameter is related to the inertial properties of aerosol particles and is generally used to describe particles larger than approximately 100 nm.

[SOURCE: ISO/TR 27628:2007, 2.2]

3.2

aerosol

metastable suspension of solid or liquid *particles* (3.29) in a gas

[SOURCE: ISO/TR 27628:2007, 2.3]