



BSI Standards Publication

**Nanotechnologies - Use and application of
acellular in vitro tests and methodologies
to assess nanomaterial biodurability**

National foreword

This Published Document is the UK implementation of ISO/TR 19057:2017.

The UK participation in its preparation was entrusted to Technical Committee NTI/1, Nanotechnologies.

A list of organizations represented on this committee can be obtained on request to its secretary.

This publication does not purport to include all the necessary provisions of a contract. Users are responsible for its correct application.

© The British Standards Institution 2017
Published by BSI Standards Limited 2017

ISBN 978 0 580 95810 6

ICS 07.120; 07.030

Compliance with a British Standard cannot confer immunity from legal obligations.

This Published Document was published under the authority of the Standards Policy and Strategy Committee on 30 November 2017.

Amendments/corrigenda issued since publication

Date	Text affected
------	---------------

TECHNICAL REPORT

ISO/TR
19057

First edition
2017-10

Nanotechnologies — Use and application of acellular in vitro tests and methodologies to assess nanomaterial biodurability

*Nanotechnologies — Utilisation et application des tests in vitro sur
cellules et méthodes pour évaluer la biodurabilité des nanomatériaux*



Reference number
ISO/TR 19057:2017(E)

© ISO 2017



COPYRIGHT PROTECTED DOCUMENT

© ISO 2017, Published in Switzerland

All rights reserved. Unless otherwise specified, no part of this publication may be reproduced or utilized otherwise in any form or by any means, electronic or mechanical, including photocopying, or posting on the internet or an intranet, without prior written permission. Permission can be requested from either ISO at the address below or ISO's member body in the country of the requester.

ISO copyright office
Ch. de Blandonnet 8 • CP 401
CH-1214 Vernier, Geneva, Switzerland
Tel. +41 22 749 01 11
Fax +41 22 749 09 47
copyright@iso.org
www.iso.org

Contents

Page

Foreword	v
1 Scope	1
2 Normative references	1
3 Terms and definitions	1
4 Symbols and abbreviated terms	2
5 Background including need for assessing the biodurability of particles	4
6 Aims and objectives	6
7 Approaches for assessment of micrometre mineral particle and fibre biodurability	6
7.1 General	6
7.2 Dissolution of nanomaterials versus their dispersion and biodegradation	7
8 Need for the assessment of nanomaterial biodurability	7
9 Influence of different types of ligands and coatings on nanomaterial biodurability	8
10 Review of methodologies to assess micrometre mineral particle and fibre biodurability	8
10.1 General	8
10.2 <i>In vitro</i> acellular methods	8
10.3 Description of different simulated physiological media	9
10.3.1 General	9
10.3.2 Simulated lung airway lining fluids	9
10.3.3 Simulated lung macrophage phagolysosomal fluid	10
10.3.4 Digestive system (saliva, gastric and intestinal fluids)	10
10.3.5 Simulated sweat (SSW)	11
10.4 Description of different simulated environmental media	11
10.4.1 General	11
10.4.2 Simulated natural freshwaters	11
10.4.3 Simulated seawater	11
10.4.4 Simulated estuarine waters	11
10.5 Description of different test systems to assess dissolution of particles and fibres	11
10.5.1 General	11
10.5.2 Static dissolution system	12
10.5.3 Continuous flow system (CFS)	12
10.5.4 Batch and batch filter systems	12
10.5.5 Tangential flow filtration system	12
10.6 Assessment of dissolved mass concentration post dissolution experiment	13
10.6.1 General	13
10.6.2 Techniques based on physical principles	13
10.6.3 Techniques based on mechanical concepts	14
10.6.4 Techniques based on chemical principles	15
10.6.5 Ultraviolet-visible (UV-Vis) spectroscopy	16
10.6.6 One-dimensional mathematical models	16
10.6.7 Single particle inductively coupled plasma-mass spectrometry (spICP-MS)	16
11 Calculation of micrometre mineral particle biodurability	17
11.1 General	17
11.2 Dissolution kinetics, dissolution rates, and dissolution rate constants	18
11.3 Dissolution kinetics and dissolution rate of larger particles and fibres	18
11.4 Dissolution kinetics and dissolution rate of nanoparticles	20
11.5 Assessment of halftime estimates of particles and fibres	20
11.6 Assessment of lifetime estimates for particles and fibres	21
11.6.1 General	21
11.6.2 Shrinking sphere theory	21
11.6.3 Shrinking fibre theory	22

11.7	Assessment of halftime and lifetime estimates	23
12	Examples of micrometer mineral particles and fibres where biodurability was assessed using <i>in vitro</i> acellular systems	24
12.1	Glass and asbestos fibres	24
12.2	Silicon dioxide (SiO ₂)	24
12.3	Talc	25
12.4	Tungsten oxide	25
12.5	Beryllium	25
13	Examples of nanomaterials where biodurability was assessed using <i>in vitro</i> acellular systems	25
13.1	SWCNTs and MWCNTs	25
13.2	Silver nanoparticles (AgNPs)	26
13.3	Titanium dioxide (TiO ₂)	26
13.4	Zinc oxide (ZnO)	26
14	Biodurability of ligands	27
14.1	General	27
14.2	Examples of ligands attached to particles where biodurability has been assessed	27
14.3	Methodologies to assess the biodurability of the attached ligands	27
14.3.1	General	27
14.3.2	Gel permeation chromatography (GPC)	27
14.3.3	Matrix-assisted laser desorption ionization mass spectrometer (MALDI-MS)	28
14.3.4	Attenuated total reflectance-Fourier transform infrared spectroscopy (ATR-FTIR)	28
14.3.5	Liquid chromatography coupled with mass spectrometry (LC-MS/MS)	28
15	Relationship with relevant international documents	28
15.1	Simulated sweat	28
15.2	Simulated sebum	29
15.3	Simulated lung fluids	29
15.4	Simulated digestive system fluids	29
16	Assessing the validity of assay/test systems	29
17	Biological relevance of the dissolution assay	30
18	Use of biodurability tests in risk assessment and its limitations	31
Annex A (informative) Tables of relevant information		32
Bibliography		36

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*.

Nanotechnologies — Use and application of acellular *in vitro* tests and methodologies to assess nanomaterial biodurability

1 Scope

This document reviews the use and application of acellular *in vitro* tests and methodologies implemented in the assessment of the biodurability of nanomaterials and their ligands in simulated biological and environmental media.

This document is intended to focus more on acellular *in vitro* methodologies implemented to assess biodurability and, therefore, excludes the general review of relevant literature on *in vitro* cellular or animal biodurability tests.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

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

bioaccumulation

process of accumulation of a substance in organisms or parts

[SOURCE: ISO/TR 13329:2012, 3.3]

3.2

biodegradation

degradation due to the biological environment

Note 1 to entry: Biodegradation might be modelled by *in vitro* tests.

[SOURCE: ISO/TR 13329:2012, 3.4]

3.3

biodurability

ability of a material to resist *dissolution* (3.6) and mechanical disintegration from chemical and physical clearance mechanisms

[SOURCE: ISO/TR 13329:2012, 3.5, modified]

3.4

biopersistence

ability of a material to persist in a tissue in spite of the tissue's physiological clearance mechanisms and environmental conditions

[SOURCE: EN 18748:1999]