



**SLOVENSKI STANDARD**  
**kSIST-TS FprCEN ISO/TS 21623:2017**  
**01-september-2017**

---

**Izpostavljenost na delovnem mestu - Ocena dermalne izpostavljenosti nanodelcem ter njihovim agregatom in aglomeratom (NOAA) (ISO/PRF TS 21623:2017)**

Workplace exposure - Assessment of dermal exposure to nano-objects and their aggregates and agglomerates (NOAA) (ISO/PRF TS 21623:2017)

Exposition am Arbeitsplatz - Leitfaden zur Beurteilung der dermalen Exposition an Nano-Objekten sowie deren Aggregaten und Agglomeraten (NOAA) (ISO/PRF 21623:2017)

Exposition sur les lieux de travail - Évaluation de l'exposition cutanée aux nano-objets et à leurs agrégats et agglomérats (NOAA) (ISO/PRF TS 21623:2017)

**Ta slovenski standard je istoveten z: FprCEN ISO/TS 21623**

---

**ICS:**

13.040.30      Kakovost zraka na delovnem mestu      Workplace atmospheres

**kSIST-TS FprCEN ISO/TS 21623:2017      en,fr,de**



TECHNICAL  
SPECIFICATION

ISO/TS  
21623

First edition

---

---

**Workplace exposure — Assessment  
of dermal exposure to nano-  
objects and their aggregates and  
agglomerates (NOAA)**

*Exposition sur les lieux de travail — Évaluation de l'exposition  
cutanée aux nano-objets et à leurs agrégats et agglomérats (NOAA)*

iTeh STANDARD PREVIEW  
(standards.iteh.ai)

SIST-TS CEN ISO/TS 21623:2018

<https://standards.iteh.ai/catalog/standards/sist/a0ae3df6-c6f2-41f4-9fc3-703f771bbea8/sist-ts-cen-iso-ts-21623-2018>

**PROOF / ÉPREUVE**

---

---



Reference number  
ISO/TS 21623:2017(E)

© ISO 2017

iTeh STANDARD PREVIEW  
(standards.iteh.ai)

SIST-TS CEN ISO/TS 21623:2018

<https://standards.iteh.ai/catalog/standards/sist/a0ae3df6-c6f2-41f4-9fc3-703f771bba8/sist-ts-cen-iso-ts-21623-2018>



**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
<b>Foreword</b> .....	<b>iv</b>
<b>Introduction</b> .....	<b>v</b>
<b>1 Scope</b> .....	<b>1</b>
<b>2 Normative references</b> .....	<b>1</b>
<b>3 Terms and definitions</b> .....	<b>1</b>
<b>4 Dermal exposure to NOAA — Evidence and exposure routes</b> .....	<b>4</b>
4.1 General.....	4
4.2 Source domains.....	4
4.3 Exposure routes.....	5
<b>5 Stepwise approach for assessment of dermal exposure to NOAA</b> .....	<b>6</b>
5.1 General.....	6
5.2 Step 1: Desk evaluation.....	7
5.2.1 Step 1A: Evaluation of toxicological hazard based on NOAA composition.....	7
5.2.2 Step 1B: Screening for potential risks associated with dermal exposure to insoluble (non-flexible) NOAA.....	8
5.2.3 Step 1C: Screening for potential risks associated with dermal exposure based on job title.....	10
5.3 Step 2: Observation of potential for dermal exposure.....	11
5.4 Step 3: Additional observation of worker behaviour.....	11
5.5 Step 4: Quantification of NOAA.....	11
5.6 Step 5: Evaluation and review.....	12
<b>Annex A (informative) Industries associated with use of nanomaterials or nano-enabled products</b> .....	<b>13</b>
<b>Annex B (informative) How to determine skin disruption?</b> .....	<b>16</b>
<b>Annex C (informative) DeRmal Exposure Assessment Method (DREAM)</b> .....	<b>18</b>
<b>Annex D (informative) Inadvertent ingestion exposure</b> .....	<b>24</b>
<b>Annex E (informative) Exploring dermal exposure measurements of nanoparticles</b> .....	<b>27</b>
<b>Bibliography</b> .....	<b>31</b>

## ISO/TS 21623:2017(E)

### 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](http://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](http://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](http://www.iso.org/iso/foreword.html).

ISO/TS 21623 was prepared by the European Committee for Standardization (CEN) Technical Committee CEN/TC 137, *Assessment of workplace exposure to chemical and biological agents*, in collaboration with ISO Technical Committee ISO/TC 146, *Air quality*, Subcommittee SC 2, *Workplaces atmospheres*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

## Introduction

Dermal exposure assessment explores the dynamic interaction between environmental contaminants and the skin. In contrast to inhalation exposure assessment, the assessment of dermal exposure requires a different set of exposure considerations. During the last decades, the body of knowledge with regard to dermal exposure has expanded for many types of substances, which amongst others resulted in publications for the evaluation of dermal exposure to chemical substances that can be found, for example, in CEN/TR 15278, CEN/TS 15279, and ISO/TR 14294.

Currently, engineered/manufactured nanomaterials and nano-enabled products are produced and used on a wide scale. Occupational skin exposure to these substances can have biological relevance to human health. Potential adverse effects include local skin effects, systemic toxicity following skin absorption/uptake and inadvertent ingestion through the hand-to-mouth pathway. This document provides guidance for the evaluation of potential dermal exposure to manufactured nano-objects, their agglomerates and aggregates (NOAA).

This document is a compilation of the results of a pre-normative research project, executed under Mandate M/461 for standardization activities regarding nanotechnologies and nanomaterials as issued by the European Commission. This pre-normative research gives an overview of the mechanisms of occupational dermal exposure to nanoparticles or nano-enabled products. This includes potential concomitant for intake or uptake. It is based on relevant evidence of exposure for identified job titles. Part of the pre-normative research comprised experimental work on the skin penetration of nanoparticles, transfer of nanoparticles from a surface to the skin, and exploratory work on the feasibility to quantify dermal exposure to NOAA<sup>[4]</sup>-<sup>[6]</sup>.

ITEH STANDARD PREVIEW  
(standards.iteh.ai)

[SIST-TS CEN ISO/TS 21623:2018](https://standards.iteh.ai/catalog/standards/sist/a0ae3df6-c6f2-41f4-9fc3-703f771bbea8/sist-ts-cen-iso-ts-21623-2018)

<https://standards.iteh.ai/catalog/standards/sist/a0ae3df6-c6f2-41f4-9fc3-703f771bbea8/sist-ts-cen-iso-ts-21623-2018>





# Workplace exposure — Assessment of dermal exposure to nano-objects and their aggregates and agglomerates (NOAA)

## 1 Scope

This document describes a systematic approach to assess potential occupational risks related to nano-objects and their agglomerates and aggregates (NOAA) arising from the production and use of nanomaterials and/or nano-enabled products. This approach provides guidance to identify exposure routes, exposed body parts and potential consequences of exposure with respect to skin uptake, local effects and inadvertent ingestion.

This document also considers occupational use of products containing NOAA by professionals, e.g. beauticians applying personal care products, cosmetics or pharmaceuticals, but does not apply to deliberate or prescribed exposure to these products by consumers.

This document is aimed at occupational hygienists, researchers and other safety professionals to assist recognition of potential dermal exposure and its potential consequences.

## 2 Normative references

The following documents are referred to in the text in such a way that some 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.

EN 1540, *Workplace exposure — Terminology*

ISO 18158, *Workplace air — Terminology*

## 3 Terms and definitions

For the purposes of this document, the terms and definitions given in EN 1540, ISO 18158 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

#### **agglomerate**

collection of weakly or medium strongly bound particles where the resulting external surface area is similar to the sum of the surface areas of the individual components

Note 1 to entry: The forces holding an agglomerate together are weak forces, for example, van der Waals forces or simple physical entanglement.

Note 2 to entry: Agglomerates are also termed secondary particles and the original source particles are termed primary particles.

[SOURCE: ISO/TS 80004-2:2015, 3.4]

## ISO/TS 21623:2017(E)

### 3.2

#### **aggregate**

particle comprising strongly bonded or fused particles where the resulting external surface area is significantly smaller than the sum of surface areas of the individual components

Note 1 to entry: The forces holding an aggregate together are strong forces, for example, covalent or ionic bonds or those resulting from sintering or complex physical entanglement, or otherwise combined former primary particles.

Note 2 to entry: Aggregates are also termed secondary particles and the original source particles are termed primary particles.

[SOURCE: ISO/TS 80004-2:2015, 3.5]

### 3.3

#### **dermal contact volume**

volume containing the mass of the agent that contacts the *dermal exposure surface* (3.7)

Note 1 to entry: This is equivalent to the volume of the skin contaminant layer and for practical reasons represents the volume of the compartment where the mass of the substance is all contained.

[SOURCE: CEN/TR 15278:2006, 2.2, modified — Note 1 adapted]

### 3.4

#### **dermal exposure concentration**

*dermal exposure mass* (3.6) divided by the *dermal contact volume* (3.3) or the dermal exposure mass divided by the mass contained in the skin contaminant layer

Note 1 to entry: Dermal exposure concentration is expressed in g/l or g/kg or other appropriate units as necessary.

[SOURCE: CEN/TR 15278:2006, 2.4, modified — Note 1 adapted]

### 3.5

#### **dermal exposure loading**

*dermal exposure mass* (3.6) divided by the *dermal exposure surface* (3.7) area

Note 1 to entry: For practical reasons, it can be expressed as mass of agent in an exposed part of the skin contaminant layer divided by the surface area of that part.

[SOURCE: CEN/TR 15278:2006, 2.5]

### 3.6

#### **dermal exposure mass**

mass of agent present in the *dermal contact volume* (3.3)

Note 1 to entry: For practical reasons, it is defined by the amount of agent in g present in the skin contaminant layer, or other appropriate units as necessary.

Note 2 to entry: The outcome of the process of dermal exposure, i.e. the contact, can be expressed by different parameters of exposure.

[SOURCE: CEN/TR 15278:2006, 2.6, modified — Note 1 adapted]

### 3.7

#### **dermal exposure surface**

skin surface area where an agent is present

Note 1 to entry: For practical reasons, this is represented by a two-dimensional representation of the skin contaminant layer in cm<sup>2</sup>.

[SOURCE: CEN/TR 15278:2006, 2.7]

**3.8****nanocomposite**

solid comprising a mixture of two or more phase-separated materials, one or more being *nanophase* (3.13)

Note 1 to entry: Gaseous nanophases are excluded.

Note 2 to entry: Materials with nanoscale phases formed by precipitation alone are not considered to be nanocomposite materials.

[SOURCE: ISO/TS 80004-4:2011, 3.2]

**3.9****nano-enabled**

exhibiting function or performance only possible with nanotechnology

Note 1 to entry: Potential release of NOAA from nano-enabled products is considered relevant in view of dermal exposure assessment.

[SOURCE: ISO/TS 80004-1:2015, 2.15]

**3.10****nanomaterial**

material with any external dimensions in the nanoscale or having internal structure or surface structure in the *nanoscale* (3.14)

[SOURCE: ISO/TS 80004-1:2015, 2.4]

**3.11****nano-object**

discrete piece of material with one, two or three external dimensions in the *nanoscale* (3.14)

Note 1 to entry: The second and third external dimensions are orthogonal to the first dimension and to each other.

[SOURCE: ISO/TS 80004-1:2015, 2.2]

**3.12****nanoparticle**

*nano-object* (3.11) with all three external dimensions in the *nanoscale* (3.14) where the lengths of the longest and the shortest axes of the nano-object do not differ significantly

Note 1 to entry: If the dimensions differ significantly (typically by more than three times), terms such as nanofibre or nanoplate may be preferred to the term nanoparticle.

[SOURCE: ISO/TS 80004-2:2015, 4.4]

**3.13****nanophase**

physically or chemically distinct region or collective term for physically distinct regions of the same kind in a material with the discrete regions having one, two or three dimensions in the *nanoscale* (3.14)

Note 1 to entry: Nano-objects embedded in another phase constitute a nanophase.

[SOURCE: ISO/TS 80004-4:2011, 2.12]

**3.14****nanoscale**

length range approximately from 1 nm to 100 nm

Note 1 to entry: Properties that are not extrapolations from larger sizes are predominantly exhibited in this length range.

[SOURCE: ISO/TS 80004-1:2015, 2.1]

**ISO/TS 21623:2017(E)****3.15****perioral region****perioral area**

area surrounding the mouth

Note 1 to entry: See Reference [10].

**3.16****skin contaminant layer compartment****SCL**

three-dimensional compartment on top of the stratum corneum (SC) of the human skin where sebum lipids, sweat and additional water from transepidermal water loss (TEWL) are present, including products from cornification and unshed corneocytes

**3.17****source domain****SD**

generation mechanism that determines particle emission characteristics for a particular life cycle stage

Note 1 to entry: Different mechanisms determine the emission rate, particle size distribution, source location and transport of NOAA during the various life cycle stages (synthesis, downstream use, application or treatment of products and end of life)[11].

**4 Dermal exposure to NOAA — Evidence and exposure routes****4.1 General**

The mechanisms of occupational dermal exposure and evidence for skin penetration and local skin effects have been defined in this document.

The relevance of dermal exposure to NOAA outlined in this document considers the following outcomes:

- a) potential for penetration and systemic effects;
- b) absorption by the stratum corneum (SC) and potential for local (skin) effect;
- c) inadvertent ingestion.

**4.2 Source domains**

A conceptual source-receptor framework suitable for nanomaterials and nano-enabled products has been developed. This links the source domains concept, as developed for modelling occupational inhalation exposure to NOAA[11] with the conceptual framework for dermal exposure. The dermal exposure framework describes the various pathways, underlying mechanisms, and potential consequences for NOAA contamination of the skin[12].

The source domains (SD) reflect different mechanisms of release and consequently possible different nature of released aerosols and are thus associated with the life cycle stages of NOAA.

- SD 1: During the production phase (synthesis) prior to harvesting the bulk material, point source or fugitive emission, e.g. emissions from the reactor, leaks through seals and connections, and incidental releases, can take place. In these cases, discrete nanoparticles and homogeneous and inhomogeneous agglomerates will be formed.
- SD 2: During the manufacturing of products, the handling and transfer of bulk manufactured nanomaterial powders with relatively low energy nanoparticles can be released, e.g. during collection, harvesting, bagging/bag dumping/bag-emptying, dumping, scooping, weighing, dispersion/compounding in composites, etc. However, the powders are already in agglomerated stage and high shear forces are needed for deagglomeration. Therefore, the majority of the released particles will be agglomerates.

- SD 3: During further processing or in the use phase of a ready-to-use nano-product, release can be expected during the relatively high-energy dispersion/application of
  - solid, powdery or (liquid) intermediates containing highly concentrated (>25 %) nanoparticles, e.g. pouring/injection moulding, (jet) milling, stirring/mixing. As higher shear forces can occur during high energy dispersion, de-agglomeration can occur, and
  - relatively low concentrated (<5 %) ready-to-use products, e.g. application of coatings or spraying of solutions that can form nano-sized aerosols after evaporation of the liquid phase component, usually of mixed composition.
- SD 4: During the use phase of a product or its end-of-life phase, activities resulting in fracturing and abrasion of manufactured nanoparticles-enabled end products at work sites can result in release of NOAA, e.g. a) low energy abrasion, manual sanding or b) high energy machining (e.g. sanding, grinding, drilling, cutting, shredding, etc.). High temperature processes like burning are included. In case of release, most likely multi-composed aerosols will be emitted, and in case of machining also matrix-bound nanoparticles, whereas during thermal processes nanoparticles can also be formed following nucleation and condensation of vapours.

Process conditions will determine the release process (i.e. mechanism, form, composition and level of release) and together with handling the process of skin contamination (i.e. through direct contact, deposition from the air compartment or transfer from contaminated surfaces). In addition, professional use of personal care products can result in direct contact of the product with the skin. Transformation (e.g. change in particle size distribution, agglomeration, etc. of the nanomaterial on the skin compared to the release) can occur either directly by the exposure process or route (e.g. transfer or direct contact), or during time of residence in the air compartment.

The level of exposure, either dermal exposure concentration, mass or surface area of exposed (body) location(s) will be determined by the underlying processes of release and exposure. In addition, the exposure time, characteristics of the substances and skin physiological conditions need to be considered.

SIST-TS CEN ISO/TS 21623:2018

<https://standards.iteh.ai/catalog/standards/sist/a0ae3df6-c6f2-41f4-9fc3-703f771bbea8/sist->

### 4.3 Exposure routes

ts-cen-iso-ts-21623-2018

Observational studies show that the most highly exposed body parts are the hands, and the predominating exposure pathway is nanoparticle transfer from contaminated surfaces[13]-[15]. However, deposition of airborne aerosols or direct contact with products containing NOAA can also contaminate other body parts (e.g. forearms and forehead). Laboratory experiments carried out as part of the pre-normative research, showed that transfer efficiency for nano-size particles was approximately 30 times higher than that of micron-size particles, and showed for each particle size that the higher the log-transformed loading, the lower the transfer efficiency (after accounting for particle size)[4][6]. Location of the exposure is of particular interest, since both the thickness of the SC and the density of the hair follicles varies substantially over body locations, which is an important parameter with regard to potential penetration and local effects of nanoparticles through the skin[16]-[19]. In addition to skin physiology, skin conditions and time of contact, the actual contact site is also relevant for potential inadvertent oral exposure due to hand-to-mouth contact[20].

Dermal exposure risk by industrial sector and job title are based on reported use of nanomaterials and nano-enabled products (see [Annex A](#)). No indication on the level of dermal exposure can be extracted from available information. However, based on the form of NOAA and nano-enabled products present in the work environment and the type of activities performed by the worker, it is possible to have a first indication of the potential for dermal exposure occurring at the workplace and the accompanying potential risk.

Nanoparticles on the skin can penetrate SC reaching viable epidermis using different pathways:

- a) through sweat glands and hair follicles, which is probably the most efficient way for penetration and permeation of NOAA;