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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)

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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).

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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[4]-[6].

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 https://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]

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^2.

[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, modified — Note 1 added]

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, modified — Notes 1 and 2 deleted]

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, 2.5]

3.12
nanoparticle
nano-object (3.11) with all 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]

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.

4.3 Exposure routes

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;

b) the intercellular route, which is only possible for very small NOAA (<4 nm) or in damaged skin condition;

c) the intracellular pathway is unlikely to be relevant for NOAA, but might be relevant for released (metal) ions.

Present evidence suggests that only very small particles (<4 nm) can penetrate intact skin, whereas insoluble, nonreactive particles with sizes >45 nm will not be absorbed by the intact skin. Penetration in the intermediate size ranges was only observed in the case of a disrupted skin where the barrier function of the skin was affected. Flexible/non-rigid NOAA, e.g. liposomes and micelles, especially spherical lipid structures, can deviate from this categorization since ultra-deformable liposomes, despite their nominal size of normally around 100 nm to 200 nm, can squeeze through the much narrower SC lipid bilayers due to their flexibility[21].

When handling liquid products at the workplace (e.g. by means of stirring, spraying, etc.) or due to vapour condensation, nanoscale droplets containing NOAA can be formed. Depending on the volatility of the substance, these droplets can easily evaporate or stay in the air for a longer period, and can even increase in volume over time due to condensation processes[22]. When these droplets come into contact with the skin (resulting in moistening of the skin), the chemical composition of the liquid, its skin-damaging properties and percutaneous absorption characteristics have to be taken into account, regardless of the droplets' original dimensions. Particular attention shall be given to nanoscale droplets consisting of liquid dispersions, that can release solid NOAA (e.g. metal salts) after evaporation of the solvent.

In case of exposure to metal (oxide) nanoparticles (Ni, Cr, Co, etc.) or carbon-based nanoparticles with metal catalytic residues, the potential release of ions can induce local skin effects (e.g. irritation and contact dermatitis), which can be enhanced by a relatively long time of residence in case of penetration of NOAA into the hair follicles. Allergic contact dermatitis is expected for certain types of nanoparticles, yet not much data exists in the peer-reviewed literature[23].

The integrity of SC and its damage due to pre-existing disease and other work-related conditions (e.g. wet work and abrasion) can be assessed relatively easily with subjective assessment methods, including questionnaires (see Annex B). Biophysical measurements of skin barrier, for instance measuring transepidermal water loss (TEWL), can have some utility in the workplace but methods are not well established. Currently, no data are available to evaluate the potential for oral intake of NOAA due to hand-mouth contact. It is assumed that determinants of inadvertent ingestion of NOAA do not differentiate from those for conventional chemicals, which means that inadvertent ingestion exposure by indirect contact depends on

— the mass loading of substance on hand or object,

— the transfer efficiency from hand or object to the perioral area (proportion),

— transfer efficiency from the perioral area to the oral cavity (proportion),

— the surface area of the hand or object involved in contact (proportion), and

— the frequency of hand- or object-to-perioral contacts.

5 Stepwise approach for assessment of dermal exposure to NOAA

5.1 General

The assessment of dermal exposure to NOAA shall begin with an initial screening assessment considering the following:

— identification of hazards;

— identification of who is involved and how;

— evaluation of risks and decisions on precautions;

— recording of significant findings;

— review of risk assessment and update if necessary.

With respect to assessment of dermal exposure to NOAA in the workplace, a stepwise approach is presented to assess the situation in the workplace in a systematic manner with a focus on

— potential for exposure based on a potential for release, and

— potential for skin disruption.

In Figure 1, an overview of this stepwise approach is given. After each step, a conclusion shall be made whether the situation at the workplace is considered to be safe based on the information that is gathered during that part of the assessment. If the situation is not considered to be safe, one shall proceed to the following step of the assessment.

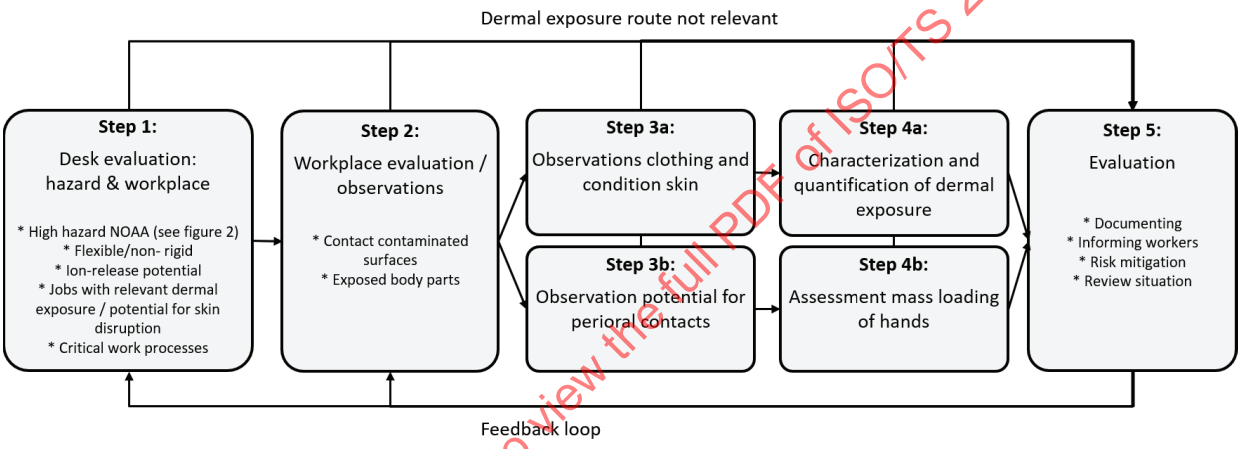


Figure 1 — Overview of stepwise approach for assessment of dermal exposure to NOAA

Below, for each of the steps more details are given, as well as a tool to perform that particular part of the assessment in practice. Where relevant, "traffic light" colours are applied in Figures 1, 2 and 3 to indicate the level of concern with regard to the (potential) risk (green = no or low concern, orange = moderate concern and red = high concern). Each step in the approach can result in a conclusion that dermal exposure to NOAA is not considered to result in a health risk for workers, after which one proceeds to step 5 (evaluation).

5.2 Step 1: Desk evaluation

5.2.1 Step 1A: Evaluation of toxicological hazard based on NOAA composition

Step 1A consists of a primary (desk) evaluation of the occurrence of possible health risks based on the NOAA composition/characteristics. In Figure 2, a schematic overview of this evaluation and the further course of the overall assessment is given.

Attention shall be given to

— metal NOAA, since the potential release of ions can induce local skin effects (e.g. irritation and contact dermatitis) and absorption of toxic or sensitizing metals,

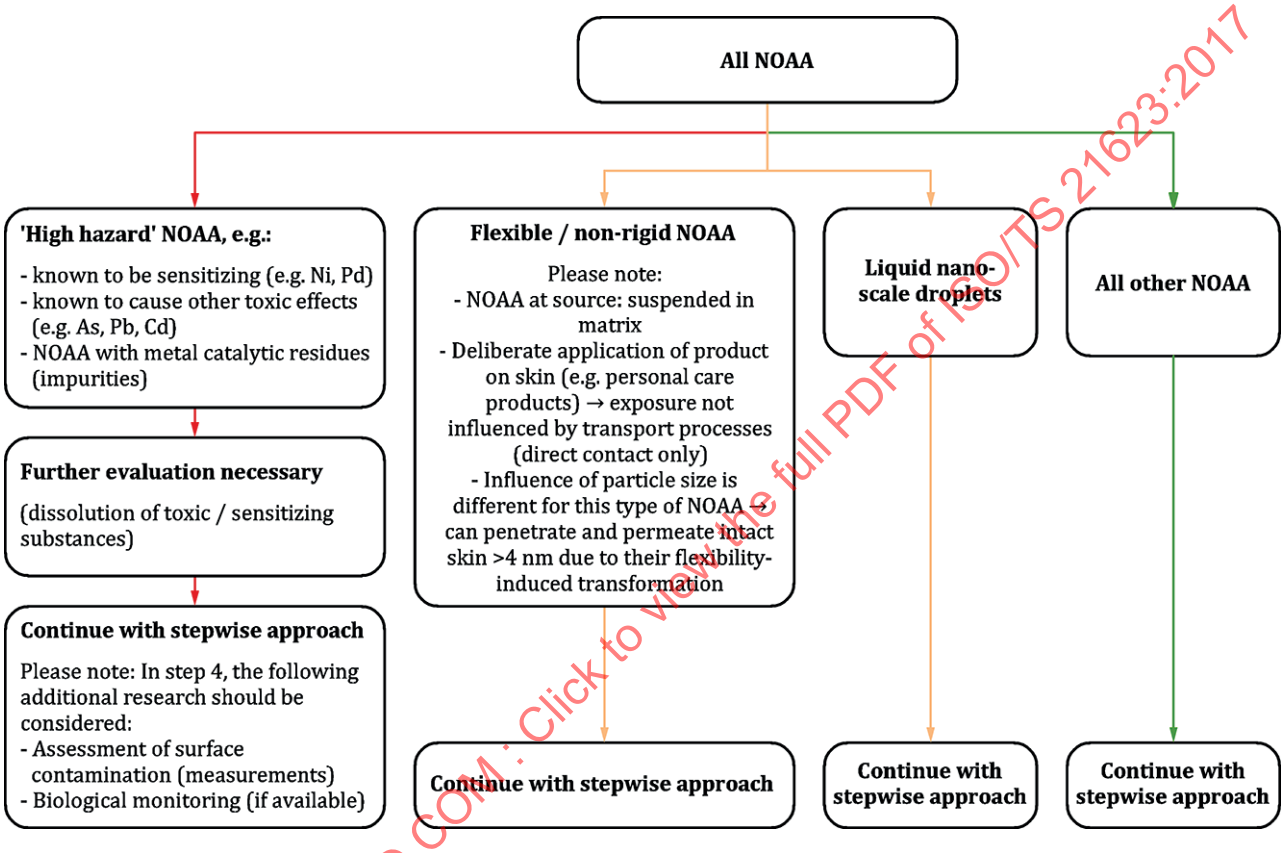
— NOAA with metal catalytic residue, since potential release of ions can induce local skin effects (e.g. irritation and contact dermatitis) and absorption of toxic metals,

— flexible/non-rigid NOAA, since due to their flexibility liposomes and micelles can penetrate and permeate the intact skin at sizes >4 nm,

— liquid nanoscale droplets containing emulsified or dissolved NOAA, which can act as discrete nano-objects, either directly or after evaporation of the solvent, and

— other toxic substances, e.g. carcinogenic substances, mutagenic substances.

In case of "high hazard" NOAA, further evaluation as part of step 1A is necessary. Dissolution of toxic or sensitizing substances in synthetic sweat shall be evaluated under physiological relevant conditions (e.g. at 32 °C to mimic the temperature of the hands).



NOTE Arrows in colour indicate variation in level of concern with regard to (potential) risk: Green means no or low concern, orange means moderate concern and red means high concern.

Figure 2 — Schematic overview of primary evaluation based on composition of NOAA and following steps

5.2.2 Step 1B: Screening for potential risks associated with dermal exposure to insoluble (non-flexible) NOAA

For relevant scenarios, screening for potential risks associated with dermal exposure to insoluble (non-flexible) NOAA shall be performed by means of an initial (desk) assessment. This screening shall be performed based on the scheme as presented in Figure 3.

Figure 3 illustrates a conceptual model for the assessment of potential risks due to exposure to NOAA in various scenarios. At the left hand side of the figure, the lines provide a simplified overview of the relevant phases of the process of screening for potential risks. It starts with indicating which source domains can be involved, and the relationship of these source domains with a characterization of the released NOAA based on the relevant release mechanism(s). Next, it indicates which would be the major mechanisms for transport of the NOAA to the skin surface and the related potential for alteration of the NOAA with regard to size. The next part of the figure shows the potential for skin exposure, both

with regard to exposure level and body location. Depending on the estimated particle size (i.e. initial particle size in combination with possible alterations during transport), the type of NOAA (metal or non-metal) and the conditions of the skin, the potential for either skin penetration or the occurrence of local effects can be estimated. Based on evaluation of exposure literature, it is assumed that only in case of direct deposition of relatively low concentrations of NOAA from the air compartment, the initial size distribution during release will not be affected[4],[5]. In this situation, there is a potential for the presence of NOAA with particle sizes below 20 nm, which results, depending on the condition of the skin, in a potential for direct penetration of the NOAA through the skin. For other scenarios, skin penetration is considered to be irrelevant and the major risks would be local skin effects due to release of Me-ions or inadvertent ingestion. Note that flexible NOAA, e.g. micelles and liposomes, are excluded from this scheme.

As is shown in Figure 3, internal exposure (uptake) of NOAA due to the dermal route is very specific and mainly relevant for either very small NOAA or the occurrence of disrupted skin. Otherwise uptake of NOAA due to inadvertent ingestion is the main route of exposure.

All possible (combinations of) exposure processes and critical sizes shall be considered when applying the scheme. In case this screening step results in "negligible or no skin penetration" and no flagged job titles are present (see step 1C), there is no need to proceed to the next step in the stepwise approach.

NOTE 1 In Figure 3, "traffic light" colours are used to indicate variation in level of concern with regard to (potential) risk: Green means no or low concern, orange means moderate concern and red means high concern. Blue is used for two phases (horizontal lines) in the scheme to indicate in what form NOAA are available (either at the source or on the skin).

All of the possible exposure processes and critical sizes should be considered. In case of metal NOAA, the "metal NOAA" path as well as the size paths should be followed.

NOTE 2 Relevant release mechanisms include among others (the influence of) pressure, forces, abrasion and heat. In general, it is assumed that for instance if high pressure/forces/heat is applied, the potential for release of NOAA is also high.

NOTE 3 Proposed critical size categories are based on experimental data[4][6].

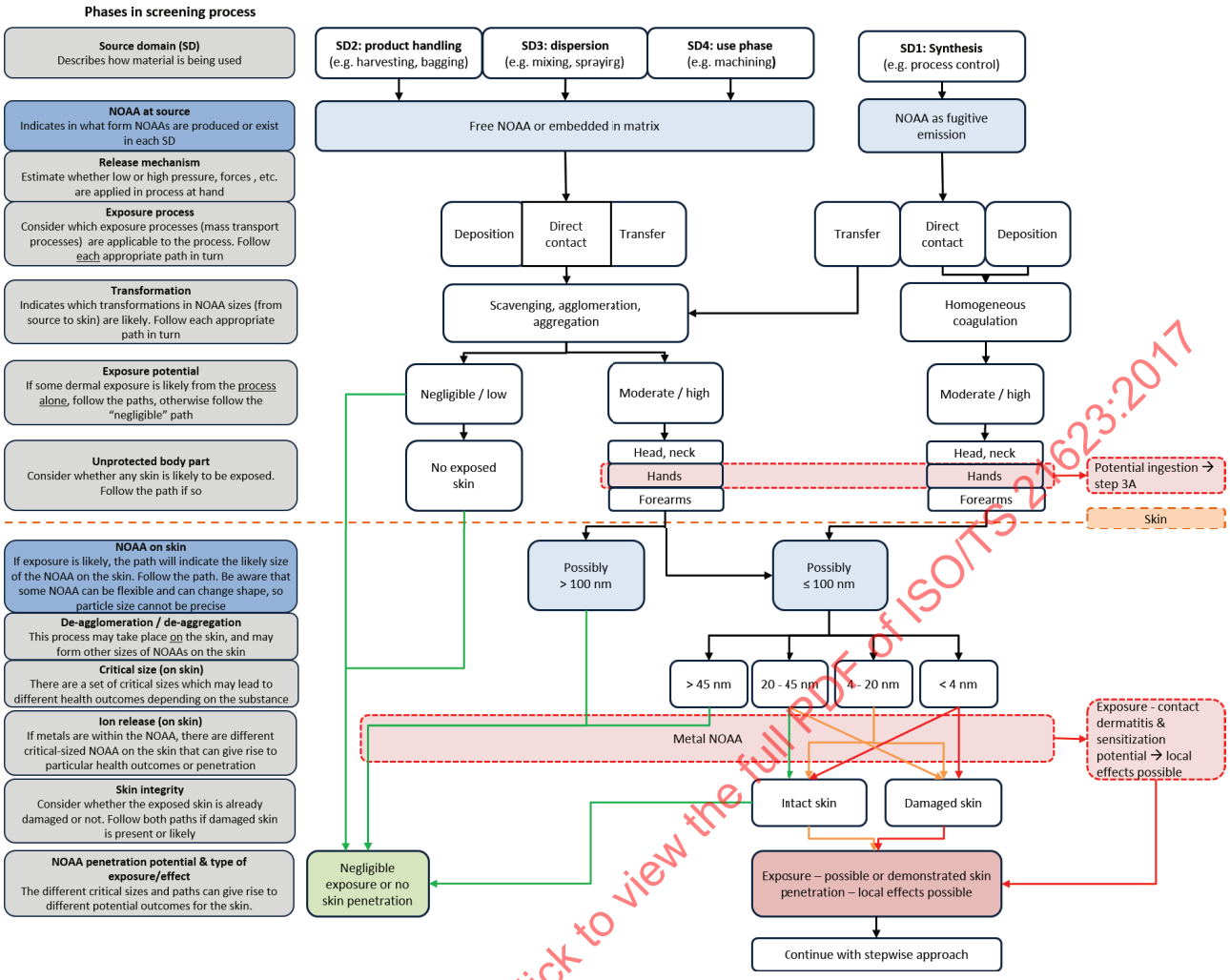


Figure 3 — Scheme for screening for potential risks associated with dermal exposure to insoluble (non-flexible) NOAA

5.2.3 Step 1C: Screening for potential risks associated with dermal exposure based on job title

For relevant scenarios, screening for potential risks associated with dermal exposure to NOAA shall be performed by means of an initial (desk) assessment. This screening shall be performed based on

— job titles with relevant dermal exposure to NOAA, and

— in case of relevant dermal exposure to NOAA, job titles with high risk of skin disruption (see Table 1);

Table 1 — Job titles with high risk for skin disruption in sectors with known use of nanomaterials (non-exhaustive)

Sector	Job title	Example of nanomaterials/products
Health care	Dental practitioner/assistant/technician	Nanocomposites
	Nurses	Pharmaceuticals containing nanomaterials
Personal care	Hairdresser	Variety of personal care products
	Beauticians/cosmetician	Variety of personal care products
NOTE Job titles with reported high incidence of skin diseases were linked to reported use of nanomaterials or nano-enabled products or exposure to NOAA to flag potential high-risk job titles with respect to dermal exposure[4].		

Table 1 *(continued)*

Sector	Job title	Example of nanomaterials/products
Construction	Construction painters	Coatings, paints
	Concrete repair workers	Mortars
Cleaning	Cleaners	Cleaning and dirt repellent coatings
Automotive	Car (body) repair workers	Primers, paints, nanocomposites
NOTE Job titles with reported high incidence of skin diseases were linked to reported use of nanomaterials or nano-enabled products or exposure to NOAA to flag potential high-risk job titles with respect to dermal exposure[4].		

5.3 Step 2: Observation of potential for dermal exposure

Additional observations of worker behaviour shall indicate where there is potential for dermal exposure (or inadvertent ingestion). These observations provide a first indication of the frequency of contacts with materials and surfaces and on exposed body parts.

The DeRmal Exposure Assessment Method (DREAM) can be used to assess the potential for dermal exposure by a structured observational approach, either in its complete form[1] or in a simplified form[15], as well as other methods or models as they become available. The DREAM method focuses on identification of the main exposure processes and main body parts involved. More information about DREAM is given in Annex C. If there is potential for dermal exposure based on these observations, proceed to step 3a and 3b.

5.4 Step 3: Additional observation of worker behaviour

a) An observational assessment shall be made to check the appropriate *use of work clothing and/or protective clothing and gloves*. Appropriate use includes the proper fit, check on uncovered body surface, consistent use over work tasks and proper removal[24]. In addition, the *condition of the skin* shall be checked with respect to the presence of cuts, redness, swelling, oozing/crusting, thickening, cracking and dryness. Subjective evaluation methods, for instance, the modified Hand Eczema Severity Index (HECSI) (see Annex B) could provide a simple tool to assess skin barrier function in relation to the likelihood of dermal uptake of nanoparticles. Another option is the measurement of TEWL (see Annex B). If exposed skin areas are present and high potential for skin barrier disruption is apparent, proceed to step 4a.

b) For indications of *perioral contacts*, the method as described by Reference [25] can be used. With regard to perioral contacts (and thus inadvertent ingestion) the process of transfer (both from surfaces to the hands, from hands to the perioral region and from contaminated objects to the perioral region are important. More information about the conceptual model integrating dermal exposure and inadvertent ingestion[20] and the ingestion exposure assessment tool (IEAT) can be found in Annex D. If there is potential for perioral contacts, proceed to step 4b.

5.5 Step 4: Quantification of NOAA

Although not considered obligatory, quantification of NOAA is considered to be a valuable addition in this stepwise approach. The type of quantification depends on the exposure route.

a) Characterization and quantification of dermal exposure to NOAA in the context of potential uptake through the skin requires a sophisticated sampling (e.g. tape lifting) and detection methods (e.g. electron microscopy of samples lifted from the skin). Appropriate methods are needed to ensure key information with regard to size and morphology can be assessed (see Annex E). If skin penetration has the potential to occur, the use of samples lifted from the skin combined with scanning electron microscopy (SEM) analysis is recommended to *characterize* the NOAA on the skin in terms of *size, morphology, and chemical composition*. However, the electronic microscopy (EM) analysis of samples lifted from the skin by tape lifts technique is currently still very challenging.

b) If there is potential for perioral contacts, an indication of the mass loading of the hand(s) and/or perioral region can be assessed by applying conventional removal methods as described in

CEN/TS 15279 and ISO/TR 14294. Alternatively, surface wipes can be used for an indication of the surface loading.

In case of high hazard NOAA that dissolve in synthetic sweat (see step 1A), it is advised to also evaluate the level of contamination of surfaces (benches, tools, etc.) in the workplace by means of surface wipes. In addition, it is advisable to evaluate the internal exposure to these substances by means of biological monitoring (if available, e.g. for As, Cr, Co, Ni in urine) for exposed workers as part of the risk assessment[26]-[29]. Please note that in case of biomonitoring, no distinction can be made between the (relative) contribution of all exposure routes (dermal, oral or inhalation). However, this information is considered relevant in relation to systemic health effects.

5.6 Step 5: Evaluation and review

It is important to evaluate the outcome of the risk assessment. This includes prioritization of the risks, formulating an action plan for risk mitigation, documenting the findings and the action plan (if relevant), and informing the workers involved about the outcome and actions. Furthermore, few workplaces stay the same. Introducing new equipment, substances and procedures could lead to new hazards. Therefore, the risk assessment shall be reviewed at appropriate time intervals, and updated if necessary, including the assessment of dermal exposure to NOAA (feedback loop).

Annex A
(informative)

Industries associated with use of nanomaterials or nano-enabled products

In order to get an overview of the industrial sectors where nanomaterials and nano-enabled products are most frequently manufactured and used, a literature search was conducted to identify national and international surveys and reviews investigating this topic. Based on this literature search, the use of NOAA seemed to be more widespread in some of the sectors (for instance ICT/Electronics, healthcare, construction, surfaces and coatings, textiles and shoes, cosmetics and personal care, automotive/automobile) than in others, indicating that the number of workers (potentially) exposed to NOAA will probably be the highest in these sectors as well[4].

Table A.1 — Industries associated with use of nanomaterials or nano-enabled products (list is non-exhaustive)

Sector/industry	Product
Information and communications technology/electronics	Electronics, computers (incl. display), electrotechnics, electronical devices, information and communications technology (ICT)
	Sensors, microelectronics
	Magnetics and magnetic materials
	Quantum computing
	(Lithium-ion) batteries
	Lights
Energy and environment/ green nanotechnology/ energy applications	(Renewable) energy
	Fossil fuel power plants
	Power-energy storage, distribution and transmission
	Water purification, filtration and desalination
	Sensing
	Environmental remediation/air emissions reduction
	Catalysis
	Photovoltaics
	Optics and optical devices
	Natural and green products
	Photonics and photonic devices
Healthcare	Nanomedicine: drug-delivery vehicles, contrast agents and diagnostic devices
	Textiles for medical applications
Aerospace/aviation	Aerospace/aviation

Table A.1 *(continued)*

Sector/industry	Product
Construction	Cement/concrete/production of wet concrete/concrete repair/concrete prefab
	Steel
	Wood
	Milling machines
	Applications for construction
	Insulation material
	Coatings and paint
	Infrastructure
	Masonry and building materials
Stone	—
Surfaces and coatings	Coatings (paints), surface coating surface modification
	Paint production
	Polish (other)
	Painters/coaters
Ceramics and glass	Ceramics and glass production/application
Security/defence	Security/defence
Chemical industry	Sustainable chemistry – catalysts
	Chemicals industry (production)
Food industry	Food production, processing, safety and packaging
	Nutrition
Textiles	Textiles
	Shoes
	Shoe repair shops
	Textile cleaning
Cosmetics/personal care	Sunscreens
	Cosmetics (production)
	Cosmetics and personal care products
Sports	Clothing/shoes
	Sports appliances/goods/equipment
Watches/optics	—
Paper industry	Paper (production)
Printing and packaging	Ink and toners (production)
Plastics	Plastics and synthetics production
	Composites in plastics/synthetics
Cleaning	Cleaning products
	Air freshener/spray

Table A.1 *(continued)*

Sector/industry	Product
Automotive/automobile	Automotive/automotive panels/motor vehicles
	Tire production
	Car body repair
	Car garages
	Lubricants
	Tires
	Fuel/diesel
	Car window
	Shock absorber
Trade/retail	Trade/retail
Metal industry	—
Home and garden	Home and garden (incl. paint)
	Household products – home improvement
Agriculture	Pesticides/plant protection products
	Fertilizers
	Super absorber
	Agriculture
Production/ manufacture of nanomaterials	Powder production
	Manufacture of nanomaterials
	Manufacture of materials (intermediates)
	Manufacture of dyes and pigments
	Manufacture of other inorganic basic chemicals n.e.c.
	Manufacturers of plastics in primary forms
Research and development (general)	Research and development (general)
Miscellaneous	Miscellaneous
	Assembly/recycling
	Appliances
	Goods for children
	Reinforced composites
	Anti-oxidants
	Absorbents

Annex B
(informative)

How to determine skin disruption?

B.1 General

Assessment of skin condition can be made by visual examination, which may include questionnaires or scoring systems, like the Nordic Occupational Skin Questionnaire (NOSQ-2002)[30] the Hand Eczema Severity Index (HECSI)[31][32] the Manuscore[31] the Osnabrück Hand Eczema Severity Index (OHSI)[31] and Hand Eczema Score for Occupational Screenings (HEROS)[33]. Furthermore, there are a number of biophysical parameters that can be used to objectively assess skin condition, like TEWL from the skin surface, skin hydration and quantitative measurement of skin colour[4].

When determining the level of skin disruption, one should take into account that what is observed at the level of individual workers cannot be directly translated to an assessment of skin disruption on a group level, since one should also take into account accidental damage of the skin that might be directly related to work. On the other hand, combining data generated on an individual level can generate valuable information on group level, and it is thus advised to document/store these observations at company and/or industry level to be able to derive for instance generic trends on group level.

B.2 Example of questionnaires

For the purpose of determining skin disruption at the workplace, it is suggested to modify the original Hand Eczema Severity Index (HECSI)[32] to be able to consider only irritative aspects (fissures and scaling) and adding "dryness" as a clinical sign.

Each hand is divided into five areas (fingertips, fingers (except the tips), palm of hand, back of hands, wrists).

For each of these areas the intensity of the three clinical signs related to impairment of the skin (fissuring, scaling and dryness) are graded following the original scale:

a) mild disease;

b) moderate disease;

c) severe disease.

For each area (total of both hands), the affected area (extent) is given a score from 0 to 4 (0 = 0 %, 1 = 1 % to 25 %, 2 = 26 % to 50 %, 3 = 51 % to 75 %, 4 = 76 % to 100 %).

The score obtained for the extent of each area is multiplied by the sum of the clinical signs for that area. The total sum of all five areas presents the skin disruption score index (SDSI), varying from 0 to 180.

Table B.1 — Scoring of skin condition to obtain skin disruption score index (SDSI)

Clinical signs/ area	Fingertips	Fingers (except tips)	Palm of hands	Back of hands	Wrists
Fissures (F)					
Scaling (S)					
Dryness (D)					
SUM (F+S+D)					
Extent (Ex)					
Area Score (AS) (SUM*Ex)	$AS_{fingertips}$	$AS_{fingers}$	AS_{palms}	AS_{backs}	AS_{wrists}
Skin disruption score index (SDSI)	$AS_{fingertips} + AS_{fingers} + AS_{palms} + AS_{backs} + AS_{wrists}$				

EXAMPLE A worker with severe fissures on the whole back of both hands and moderate scaling and dryness on the whole palm of the right hand would have an SDSI of 20 (out of 180).

Table B.2 — Worked example

Clinical signs/ area	Fingertips	Fingers (except tips)	Palm of hands	Back of hands	Wrists
Fissures (F)	0	0	0	3	0
Scaling (S)	0	0	2	0	0
Dryness (D)	0	0	2	0	0
SUM (F+S+D)	0	0	4	3	0
Extent (Ex)	0	0	2	4	0
Area Score (AS) (SUM*Ex)	0	0	8	12	0
Skin disruption score index (SDSI)	0 + 0 + 8 + 12 + 0 = 20				

B.3 Measurement of transepidermal water loss (TEWL)

The stratum corneum (SC) contributes greatly to skin barrier function and transepidermal water loss (TEWL) is a non-invasive *in vivo* measurement of water loss across the SC[34]. It is raised in subjects with atopic dermatitis (AD)[35] and with impaired skin barrier[36]. TEWL recording is strongly influenced by room temperature and sweating, but in controlled conditions TEWL can be a marker of impaired skin barrier[37]. The measurements can be carried out using an open or close chamber system.

The subject's arm needs to be acclimated before measurement by exposing the arm in a climate controlled room for 10 min in which both temperature and humidity are maintained constant by an air conditioning system. Temperature shall be set in the range from 20 °C to 23 °C with relative humidity maintained in the range from 30 % to 45 %. TEWL shall be taken on the lower volar surface of the forearm or on the back of the first finger by applying a probe to the exposed skin for approximately 15 s. The limitation of this method is the wide inter-subjects variability and the absence of accepted normal range values.

Annex C
(informative)

DeRmal Exposure Assessment Method (DREAM)

DREAM is an observational method to assess dermal exposure to chemical agents in a semiquantitative manner[38]. DREAM closely follows the conceptual model of Schneider et al.,[12] and presents an initial dermal exposure assessment with the possibility to rank tasks or jobs. The model is implemented in a MS-Access database. DREAM consists of two parts, an inventory and an evaluation part. In the inventory part of DREAM, the relevant determinants are grouped under six main modules (see Table C.1). Information about the direction and magnitude of the effect of the included determinants has been collected from literature and supplemented with expert judgement. The modules used in DREAM are not explicitly defined by the transport processes described in the underlying conceptual model, but in a more pragmatic manner to suit the observational character of the model. An occupational health professional collects information about the company, characteristics of the substances used, cleanliness of the environment, personal hygiene, protective clothing and exposure duration by observing the process and interviewing the workers. The investigator estimates the "probability" and "intensity" of a certain exposure route and the distribution of exposure over the different body parts.

Table C.1 — DREAM groups determinants in modules

Module		Description
Company module		General information about company and observer
Department module		Presence of source and surface contamination layer. Cleaning (decontamination) activities at department.
Agent module		Intrinsic emission; physical characteristics
Exposure module	*Exposure routes*	Probability and intensity of exposure routes
	Clothing estimate	Use and efficacy of (protective) clothing
Task module		Duration of task
Job module		Drivers; workers hygiene, continued exposure

DREAM consists of an inventory and an evaluation part. The inventory part comprises a hierarchically structured multiple choice questionnaire with six modules: company, department, agent, job, task and exposure. The questionnaire is to be filled in while or after observing workers performing their tasks. However, when not feasible, information can be obtained by interviewing workers. The questionnaire addresses factors such as:

— probability (P) and intensity (I) of dermal exposure processes (emission (direct contact), deposition, transfer);

— factors for nine body parts;

— clothing layer (CL_{PF});

— physical and chemical characteristics of agent (E_J);

— percentage of total working time a task is performed (WT).

In the evaluation part, potential and actual dermal exposure levels are estimated in DREAM units based on the information gathered with the inventory. The estimation of the potential dermal exposure level is based on the product of "probability" and "intensity" of each exposure route and corrected for 33 determinants at task level (see Table C.2).

After inclusion of protective clothing and gloves, actual exposure is calculated. DREAM estimates exposure for nine separate body parts. Figure C.1 gives an overview of the evaluation part of DREAM. Both the inventory by means of the questionnaire and following evaluation are integrated into an Access tool.

Table C.2 — Overview of determinants per module

Determinant	Category	Rationale
Exposure module — Exposure routes		
1. Emission to clothing and uncovered skin; and immersion of skin into agent	Unlikely (<1 % of task duration) Occasionally (1 % to 10 % of task duration) Repeatedly (>10 % to 50 % of task duration) Almost constantly (>50 % of task duration)	Increasing frequency results in higher exposure levels
2. Intensity (= amount of agent) of emission	Small amount (<10 % of body part) Medium amount (10 % to 50 % of body part) Large amount (>50 % of body part)	Increasing amount of agent results in higher exposure levels
3. Exposure route factors for emission (ER_E), deposition (ER_D) and transfer (ER_T)	ER_E ER_D ER_T	In the underlying model, emission starts at higher exposure levels than deposition and transfer
4. Probability of deposition on clothing and uncovered skin	Unlikely (<1 % of task duration) Occasionally (1 % to 10 % of task duration) Repeatedly (>10 % to 50 % of task duration) Almost constantly (>50 % of task duration)	Increasing frequency results in higher exposure levels
5. Intensity of deposition on clothing and uncovered skin	Small amount (<10 % of body part) Medium amount (10 % to 50 % of body part) Large amount (>50 % of body part)	Increasing amount of agent results in higher exposure levels
6. Transfer to clothing and uncovered skin: Contact with surfaces, or tools, occurs	Unlikely (<1 % of task duration) Occasionally (1 % to 10 % of task duration) Repeatedly (>10 % to 50 % of task duration) Almost constantly (>50 % of task duration)	Increasing contact frequency results in higher exposure levels

Table C.2 *(continued)*

Determinant	Category	Rationale
7. Intensity of transfer: Contamination level of contact surface	Not contaminated Possibly contaminated ≤50 % of contact surface >50 % of contact surface	Increasing contamination results in higher exposure levels
8. Body surface factor	Head = 0,69 Upper arm = 0,67 Forearm = 0,53 Hands = 0,47 Torso front = 1,22 Torso back = 1,22 Lower body part = 2,43 Lower leg = 1,15 Feet = 0,63	The body part factor is defined as the surface area of an individual body part divided by the mean surface area of the nine body parts
Agent module		
9. Physical state	Solid Liquid Vapour – gaseous	Experiments comparing solids and liquids show inconsistent results, therefore both have factor 1. Solids and liquids are supposed to result in higher exposure levels than vapours and gases
10. Concentration	>90 % active ingredient of interest 1 % to 90 % active ingredient of interest <1 % active ingredient of interest	Dermal exposure increases with concentration of active ingredient in substance
11. Evaporation (liquids): boiling temperature	<50 °C 50 °C to 150 °C >150 °C	Volatile liquids result in lower dermal exposure due to increased removal
12. Viscosity (liquids)	Low (like water) Medium (like oil) High (like resin/paste)	Higher viscosity results in decreased removal from (covered) skin. Stickiness is expected to increase equally with viscosity
13. Formulation (solids)	Powder/fine particles Granules/grain/pellets/particles Pack/bunch/bundle	Adherence to skin varies inversely with particle size. Smaller particles result in higher emission, have increased transfer and have higher adherence to skin (decreased removal)
14. Dusty (solids)	No Yes	Dusty solids are emitted more easily from source than non-dusty solids
15. Stickiness/wax/moist (non-powder and non-dusty solids)	No Yes	Sticky, waxy and moist solids result in better attachment to skin and therefore in decreased removal from (covered) skin

Table C.2 *(continued)*

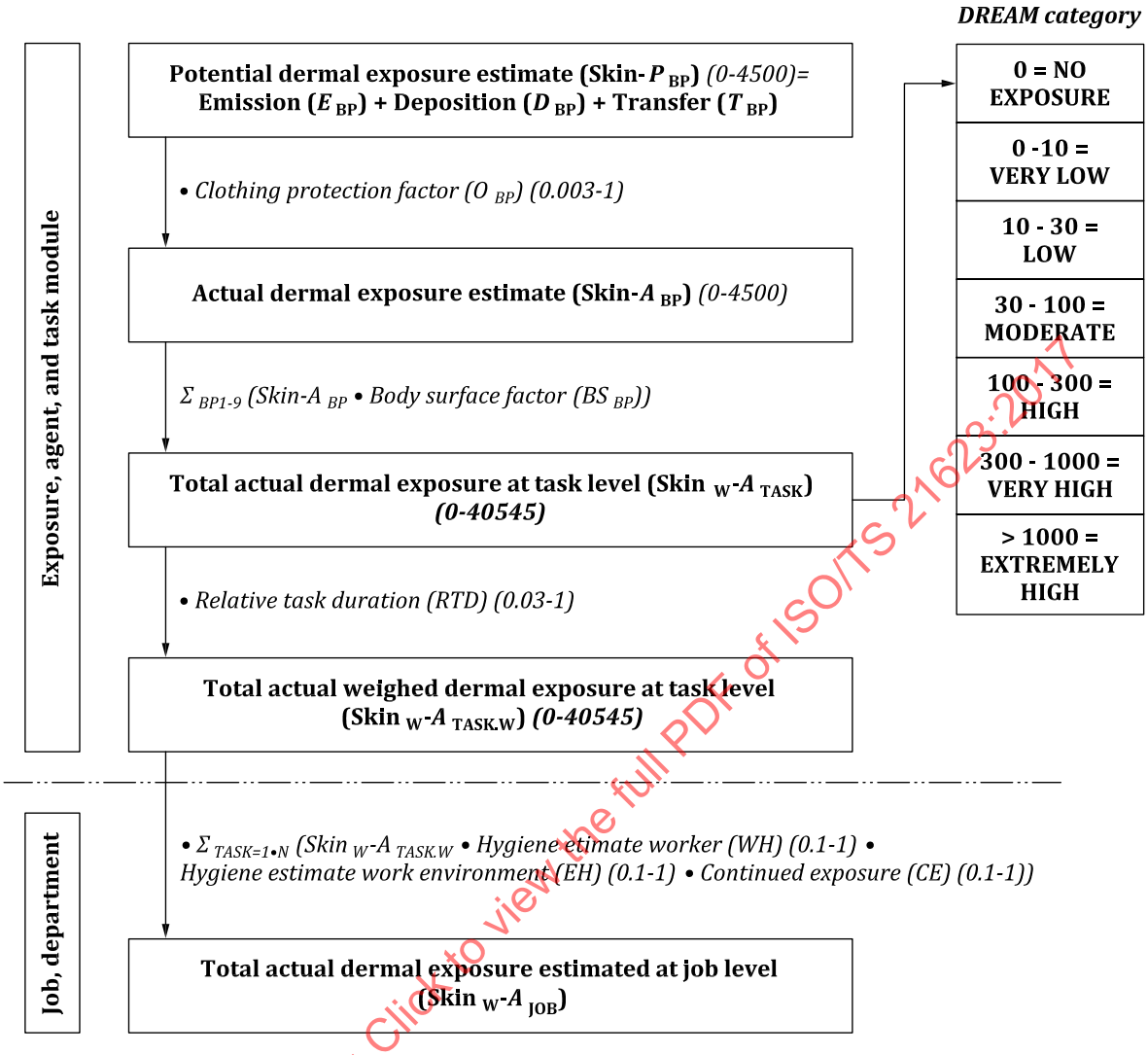
Determinant	Category	Rationale
Exposure module — Clothing factor		
16. Glove or clothing material	No gloves used/body part not covered Woven clothing Non-woven permeable Non-woven impermeable	Use of gloves (clothing) reduce(s) external dermal exposure
17. Protection factor	PFMHA (hands) PFMBP (other body parts)	Gloves experience higher pressure and friction than clothing of other body parts
18. Replacement frequency	After having them used once Daily Weekly Monthly	Gloves (clothing) that are replaced frequently reduce exposure more than gloves (clothing) that are infrequently replaced
19. If non-woven gloves connect well to clothing of arms	No Yes	Gloves connecting well reduce exposure more than gloves that do not connect well
20. If non-woven gloves are worn during	0 % to 25 % of task duration >25 % to 99 % of task duration 100 % of task duration	Gloves worn during total time of task performance reduces exposure more than gloves worn during part of the time
21. A second pair of gloves is worn under outer gloves	No Yes	Use of a second pair of gloves can reduce exposure
22. Replacement frequency of these inner gloves	After one time Daily Weekly/monthly	Inner gloves only protect if frequently replaced; if not, they become a source of exposure
23. Barrier cream used	No Yes	Use of barrier cream reduces exposure
Task module		
24a. Relative task duration: relative time of task performance = (frequency × duration task)/total working time); categorical estimate	Daily 4 h to 8 h/weekly >20 h/monthly >80 h/yearly >800 h Daily 1 h to 4 h/weekly 4 h to 20 h/monthly 16 h to 80 h/yearly 160 h to 800 h Daily 11 min to 60 min/weekly 1 h to 4 h/monthly 4 h to 16 h/yearly 40 h to 160 h Daily <11 min/weekly 0 h to 1 h/monthly 0 h to 4 h/yearly 0 h to 40 h	Increasing task duration results in higher dermal exposure
24b. Relative task duration: relative time of task performance = (frequency × duration task)/total working time); absolute estimate	Total time of task performance divided by total working time	

Table C.2 *(continued)*

Determinant	Category	Rationale
Job module		
25–26. Workers' hygiene factor determined by: hand-wash frequency and wash efficiency	Hands not washed Washed two times to 10 times per shift with water Washed two times to five times per shift (scrub) soap or solvents Washed >10 times per shift with water Washed >5 times per shift with (scrub) soap or solvents	Hand washing reduces exposure
27–29. Continued exposure = working clothes immediately changed after work × workers wash own working clothes × workers immediately shower after work	Working clothes are immediately changed after work Workers responsible for washing own working clothes: Workers immediately shower after work	Contaminated working clothes result in exposure after work; direct showering reduces continued exposure
30–33. Hygiene estimate work environment = (hygiene floor + hygiene work tables + hygiene machines + hygiene working tools/4)	Hygiene estimates of floor, worktables, machines and working tools determined by cleaning frequency and cleaning efficiency. Daily cleaning wet, or dry and wet Weekly cleaning wet, or dry and wet Cleaning dry	Higher cleaning frequency results in cleaner work environment. Wet cleaning is more efficient than dry cleaning

DREAM is an exposure assessment method and therefore not validated, but reliability and accuracy of the method were assessed. Two subsequent papers illustrated the repeatability of the assessment[39] and the accuracy of the methods[40]. They found that inter-observer agreement for ranking dermal exposure of the nine body parts was moderate to good (median values of Spearman correlation coefficients for pairs of observers ranged from 0,29 to 0,93), but correlation differed for agricultural and industrial settings. In addition, when they compared DREAM estimates with measured exposures the Spearman correlation coefficients for individual observations ranged from 0,19 to 0,82 (reasonable for hand exposure, but moderate for body exposure). For potential dermal exposure, DREAM estimates correlated less well with measurements then the DREAM estimates of actual dermal exposure. The authors concluded that the DREAM method was suitable for groups of workers with considerable contrast in dermal exposure levels. However, for scenarios with less contrasting exposure levels, quantitative dermal exposure measurements would be preferable.

In 2008, 10 European enterprises were visited during the NANOSH project to assess quantitative inhalable and semiquantitative dermal exposures to NOAA, by means of an adapted version of the DREAM observational method[15] which showed to be useful. The results of this study showed that in 30 out of the 45 observed tasks the body parts with the highest likelihood of exposure were the hands. The main routes for exposure of the hands were direct contact and transfer. The main routes for exposure of the total body were transfer and direct contact.



NOTE Each estimate is determined by a set of underlying variables[38]. The ranges of the estimates are in brackets.

Figure C.1 — Summary of the evaluation model of DREAM

Annex D
(informative)

Inadvertent ingestion exposure

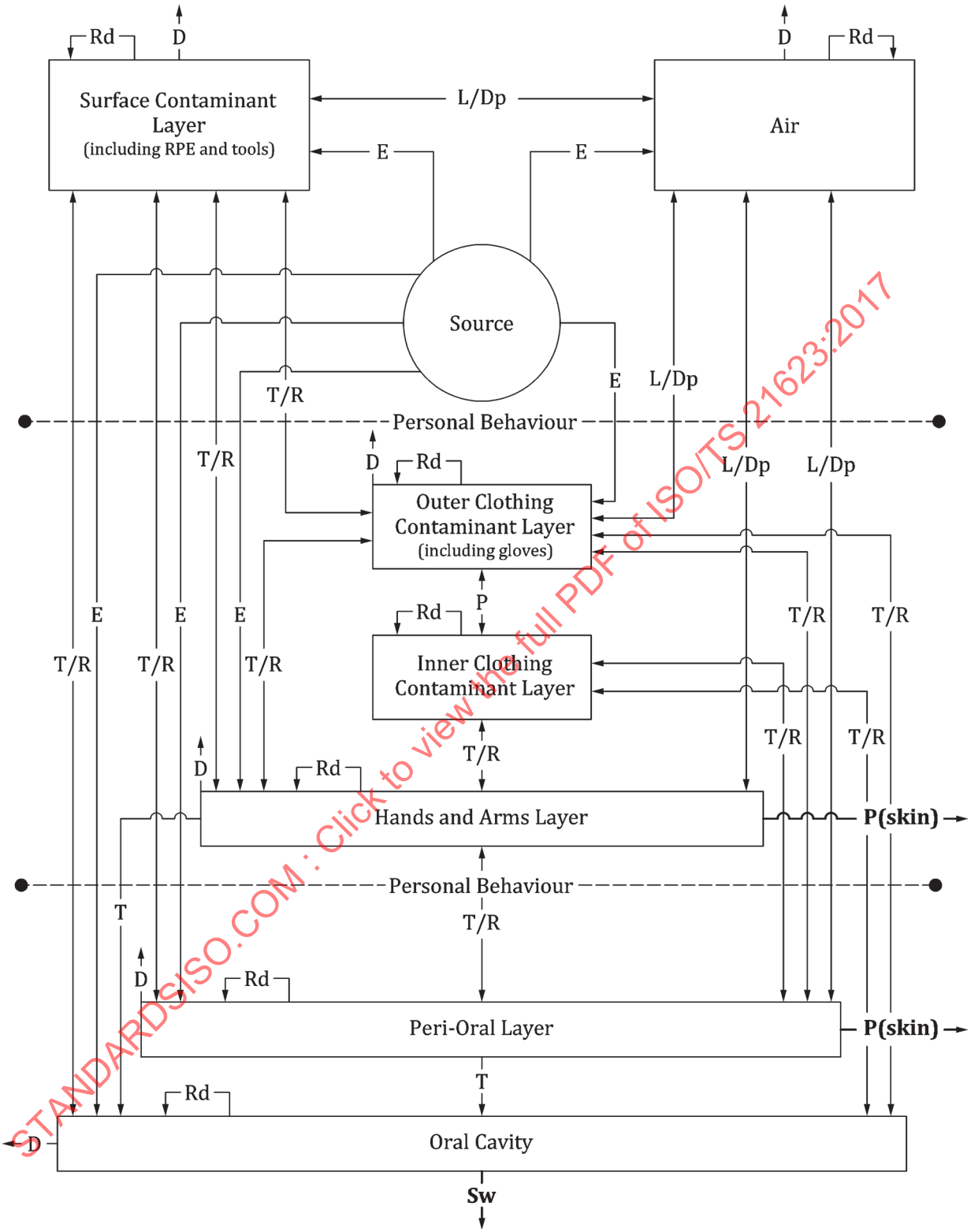
Cherrie et al.[41] and Schneider et al.[12] have published conceptual models for inadvertent ingestion and dermal exposure, respectively. The conceptual model by Cherrie et al.[41] was used by Christopher et al.[20][42] to develop an inadvertent ingestion exposure predictive model. Both conceptual models describe the transfer of contaminants between compartments via episodic events. The processes described in the two conceptual models are integrated to create a combined dermal/ingestion exposure conceptual model, which is presented in Figure D.1[20].

Inadvertent ingestion exposure was defined as the ingestion (uptake) of substances via the oral cavity, through processes of which the individual is oblivious. A simple validated model explaining the processes involved in inadvertent ingestion exposure was developed and its strong relation to dermal exposure was identified. The roles of hand-to-mouth and object-to-mouth events as the primary exposure processes were highlighted. Two exposure "compartments" were defined: the *peri*-oral area (i.e. the area of skin around the outside of the mouth) and the oral cavity. The role of human behaviour in determining inadvertent ingestion exposure was also investigated. Although requiring further development, this model showed that it can be possible to estimate inadvertent ingestion exposure.

This model has recently been updated[43] to produce an inadvertent ingestion exposure modelling tool called the ingestion exposure assessment tool (IEAT). Information was gathered through a review of the literature, laboratory experiments on dermal and oral transfer, field observations of hand-to-mouth behaviour. Information from the literature review was used to develop a database of transfer efficiencies, along with accompanying contextual information, describing the proportion of a substance that is transferred from one area to another following contact. This was supplemented with information from laboratory experiments carried out on volunteers to estimate transfer efficiencies for hand-to-mouth, glove-to-mouth, respiratory protective equipment (RPE)-to-mouth, arm-to-mouth and clothing-to-mouth contact. This database was used to help identify transfer efficiencies to be used in IEAT. Field work was carried out at a number of UK worksites both to collect hand and perioral exposure measurements and observations of hand-to-mouth contacts. The measurements were used in the validation of the IEA-model[20][44] (http://www.iom-world.org/research/research-expertise/exposure-assessment/ingestion-exposure-assessment-tool/) and also provided some useful information about inadvertent ingestion exposure. Measurements from the hands and perioral area were found to be very strongly correlated which emphasized the link between dermal and inadvertent ingestion exposure.

IEAT is a predictive exposure assessment tool that can be used to estimate occupational inadvertent ingestion exposure to liquids and solids over a full work shift. The model works best for estimating the geometric mean exposure for a group of workers with similar job patterns and need not be as effective at detecting differences between individual workers within the group. Inadvertent ingestion exposure can occur when workers touch their mouths with contaminated hands or objects while working. The model is intended to be a Tier 1 model and to be simple and easy to use. The tool estimates the mass loading of material in the perioral area (µg) and exposure to the hands (µg/cm^2). IEAT estimates perioral exposure as a surrogate for inadvertent ingestion exposure. However, the model parameters are not designed for nanomaterials, and as discussed above very small particles are likely to have markedly different transfer properties compared to larger micron-sized materials. Inadvertent ingestion exposure will also be closely correlated with hand exposure and it is probably difficult to separate the two routes of exposure in terms of association between estimated exposure and biological response.

NOTE IEAT is freely available and can be downloaded via the website of IOM (www http://www.iom-world.org/).



Key

D	decontamination	E	emission
Dp	deposition	Sw	swallowing
R	removal	T	transfer
Rd	redistribution		
L	resuspension or evaporation		

L/Dp deposition and resuspension/evaporation (opposite directions)

P penetration and permeation

T/R transfer and removal (opposite directions)

NOTE T/R between the surface contaminant layer and the oral cavity is depicted by a dashed line to indicate that transfer by this pathway is only likely to occur for surfaces that are portable and capable of being placed into the mouth.

Figure D.1 — Integrated dermal and ingestion conceptual model[20]

Annex E
(informative)

Exploring dermal exposure measurements of nanoparticles

E.1 General

A key goal in measuring deposition of nanoparticles on the skin is to retain their size and shape properties during sampling so that the hazard they present on the skin can be understood. Different dermal sampling methods exist which are selected according to the nature of the substance being sampled and the circumstances in which exposure occurs. They are usually broken down into three distinct categories of sampling technique according to CEN/TS 15279 and ISO/TR 14294, i.e. by interception, by removal and by *in situ* methods.

E.2 Interception

Sampling media are used to intercept powders or suspensions *en route* to the exposed skin. A fabric or plastic glove is placed over the hand or protective glove, or a patch of fabric or other material is laid over the skin or outer clothing. Particulates, solids or liquid suspensions are collected on the sample media over the sampling period. Usually, they are assayed by mass through recovery from the media, and the physical form on collection is not important as long as it is retained in the media. The nanoparticles need not behave in the same physical fashion (collect, agglomerate, disintegrate, etc.) when they collect on the sampling media as they would on the skin. There would be differences in electrostatic properties between skin and sampling media. Recovery from the pad after collection is a second step to detection, and this too can change the intrinsic properties for the nanoparticles and their size distribution. However, so as not to disturb the nanoparticles after they have landed, electron microscopy grade double-sided adhesive carbon tape (which is conductive and emits low VOCs) or equivalent could be used as an interception collection medium to fix them, followed by analysis under scanning electron microscope (SEM). Creams and suspensions will not be fixed in this manner, so the method is only applicable to powders. The type of adhesive tape used shall be suitable for use in an SEM. The conductivity of the tape is a critical factor because coronas can build up from the electron beam, especially under high vacuum, unless charge can be dissipated.

E.3 Removal

Nanoparticles may be washed into a liquid suspension either from skin directly (hand washing) or from pads, gloves or patches (as interception samplers above) or from skin wipes. For insoluble nanoparticles, the resulting liquid suspension can be sized by laser diffraction. This technique has been used to determine size distributions of nanoparticle suspensions[45] quoting diameters down to 90 nm. However, this suspension process would certainly change its properties compared to how those sizes would have been retained on the skin or sampler medium. Different removal efficiencies of agglomerates and individual nanoparticles into washings could strongly influence the nanoparticle size distribution so measured. For soluble nanoparticles, complete digestion or dissolution by a known volume of a solvent such as water or acid, followed by an assay of mass concentration, would yield mass as in traditional (i.e. non-NOAA) dermal exposure measurements, but would yield no surface or size information.

Adhesive tapes have been used to try to recover (lift) dust particles from the skin and from surfaces, which are then recovered for mass (see washing above) or examined under SEM without further (deliberate) disturbance. There is no reason to believe that adhesive tapes should not be able to lift nanoparticles, as well as larger dust particles, but there can be technical problems with recovering nanoparticles in representative proportions, particularly from skin. These can be associated with the