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nano risk governance

ConsExpo nano
-
Use of nano TiO_2 (NM-105) in spray painting indoors

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1 Tool description and use domain(s)

The ConsExpo nano tool can be used to estimate inhalation exposure to nanomaterials in consumer spray products. The model combines predictions of aerosol concentration in indoor air with the predictions of alveolar load in the lungs, because the duration and magnitude of the alveolar load of a nanomaterial are most critical in determining inflammation of the lungs.

To estimate the alveolar load, ConsExpo nano combines different models: first, a model to estimate inhalation of material with aerosol particles after use of a spray, and second, a model to estimated deposition and clearance of material in the respiratory tract after inhalation.

The underlying model algorithms to predict the indoor air concentrations and inhalation of aerosol particles are the same as implemented in ConsExpo Web (Delmaar et al., 2016) model for estimating inhalation of non-volatile substances in consumer sprays. To estimate deposition of the inhaled aerosol particles in the respiratory tract and clearance of the inhaled material from the alveoli, ConsExpo nano implements the ICRP model (ICRP, 1994; Gregoratto et al., 2010; Gregoratto et al., 2011).

2 Description of case study

To illustrate the use of ConsExpo nano (version 2.0), the tool is applied in a hypothetical risk assessment setting, in which exposure to nanoTiO_2 (NM105) arising from the use of a coating is assessed. ConsExpo nano is an indoor consumer exposure assessment tool. Therefore, as an example scenario, the use of a spray paint indoors is taken. It is assumed that the considered paint contains 30% nanoTiO_2.

ConsExpo nano expresses exposure as retained dose in the pulmonary (alveolar) region of the respiratory tract. An exposure event may occur repeatedly, with a certain frequency. In such a case, the event is assumed to occur in the same way every time. The total retained dose at any particular time results from the contribution of all exposure events and intermediate clearance of the deposited material from the pulmonary region.

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To better inform risk assessment, ConsExpo nano also includes a module to simulate the alveolar load in a dose-response study in rat. This module can be used to compare retained dose in humans that arise during product exposure with the retained dose in the rat at some benchmark exposure. It should be noted that this module of ConsExpo nano does not facilitate comprehensive risk assessment, but it provides valuable insight in potential risk nevertheless.

For the hazard modelling in this case study, we use, following (Fransman et al., 2017) dose-response data from an inhalation study by (Bermudez et al., 2004).

2.1 Simulation settings

In our case study we assume that effects are expected to be related to the dose per unit surface area of the alveolar region. So, we select 'per m^2 alveolar area' in the ConsExpo nano tool. This will express both human and rat doses per unit exposed alveolar surface area. ConsExpo nano provides defaults for the human and rat alveolar surface area. These may be overwritten, but are accepted for this case study.

2.2 Human exposure

For the scenario of spray painting indoors, ConsExpo nano provides a default exposure assessment, taken from the ConsExpo fact sheet on Paint Products (Bremmer & van Engelen, 2007). This scenario describes the painting of a small surface (4 m^2) in a garage, using a spray paint. The surface treatment is assumed to be repeated twice a year, every year.

The input parameters for the default assessment can be loaded into the web application using the option 'Load default scenario from factsheet', then selecting the fact sheet 'Painting Products' and finally the defaults for the 'spray can'. The loaded default input values characterize the spray product and its use in a spray application. Defaults include, for example, a specification of the sprayed aerosol (particle size distribution), the mass generation rate of the spray, the spray and exposure durations during a single event.

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2.3 Hazard study

As a reference hazard study, (Bermudez et al., 2004) is used. (Bermudez et al) conducted a 13 weeks dose response inhalation study. Animals were exposed to 0.5, 2.0, and 10 mg/m^3 uf- TiO_2 for 6 h/day, 5 days/week, for 13 weeks. Minimal hypertrophy and hyperplasia of type II alveolar epithelial cells was observed for the mid-dose group. This dose group (exposed to 2.0 mg/m^3) is modelled in ConsExpo nano to provide reference retained doses in rat for risk evaluation. It should be noted that this exposure is only used as a reference to place the human exposure in perspective. It is by no means to be considered as a benchmark of risk.

To model the retained alveolar dose for the hazard study, the experimental settings of the study need to be specified. From (Bermudez et al.), the aerosol size distribution to which rats were exposed was characterized as 1.44 µm mass median aerodynamic diameter (MMAD) with a geometric standard deviation (GSD) of 2.6. Using this specification, the multi-path particle depostion (MPPD) model (Ara, 2017) was used to estimate an overall pulmonary deposition fraction of 0.04. This was then used as input in ConsExpo nano. Exposure duration in the experiments was 13 weeks (equalling 91 days). The ConsExpo nano program default for the inhalation rate of 0.015 m^3/h was used. Finally, the specification of the nanomaterial in the Hazard module was specified in exactly the same way as that for the human exposure scenario.

3 Input parameters

A complete list of model inputs is given in table 1.

Table 1 Input of the ConsExpo nano case study

Input parameter	Value	unit
Exposure scenario		
Scenario type	'Spray Scenario'	-
Exposure duration	20	Minutes
Density aerosol	4.23	g/cm^3
Weight fraction nanomaterial in aerosol particle	1	-
Diameter distribution		
Diameter (mass median)	15.1	µm
Arithmetic coefficient of variation	1.2	

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Input parameter	Value	unit
Simulation		
Exposure pattern	Repeated (unlimited)	-
Exposure frequency	2	per year
Simulation duration	365	days
Deposition model	ICRP; Male (light exercise)	
Inhalation rate	1.4	m^3/h
Spray		
mass generation rate	0.45	g/s
weight fraction nanomaterial in product	0.3	
airborne fraction	0.7	
spray duration	900	s
room		
room volume	34	m^3
room height	2.25	m
ventilation rate	1.5	air changes per hour
nanomaterial		
density nanomaterial	4.23	g/cm^3
type of distribution	monodisperse	
shape of nanomaterial	sphere	
diameter nano particle	26	nm
density nanomaterial	4.23	g/cm^3
type of distribution	monodisperse	
Hazard study		
Air concentration	2.0	mg/m3
Aerosol diameter	1.44	µm
Density aerosol particle	4.23	g/cm^3
Number of days	91	
Exposed hours per day	4.3	hours
Simulation duration	500	days
Density nanomaterial	4.23	g/cm^3
Diameter	26	nm
Deposition fraction	0.04	
inhalation rate	0.015	m^3/h

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4 Results

ConsExpo generates different output measures. In the section 'Event doses', different dose measures of the exposure occurring in a single painting event are given. These include inhaled and deposited (i.e. in the alveolar region) doses in different dose metrics (e.g. as mass, surface area, number of particles of the nanomaterial), in the normalization we selected for our case (i.e. per m^2 alveolar surface area). In this case, we are mainly interested in the retained dose in the alveoli. This is the cumulative dose resulting from repeated use of the spray. To view the retained dose, we need to refer to the section 'dose-time plots'. Here we find plots of the retained dose in both human and rat. At the top of this section, the preferred dose metric must be selected. In this case, for local effects in the lung associated with TiO_2 exposure, we select 'surface area nano particles' as the dose metric. In combination with the normalisation we selected in the simulation settings, retained doses are now displayed as 'surface area nano particles per m2alveolar area' .

The retained dose time plots estimated for human and rate in our case are presented in Figure 1 and Figure 2.

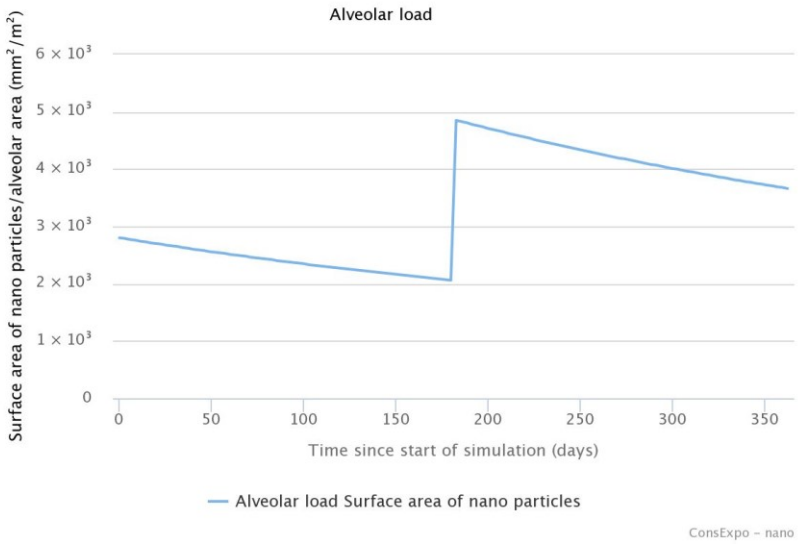

Figure 1 Estimated retained dose (alveolar load) in human after repeated use of a spray paint containing nano TiO_2

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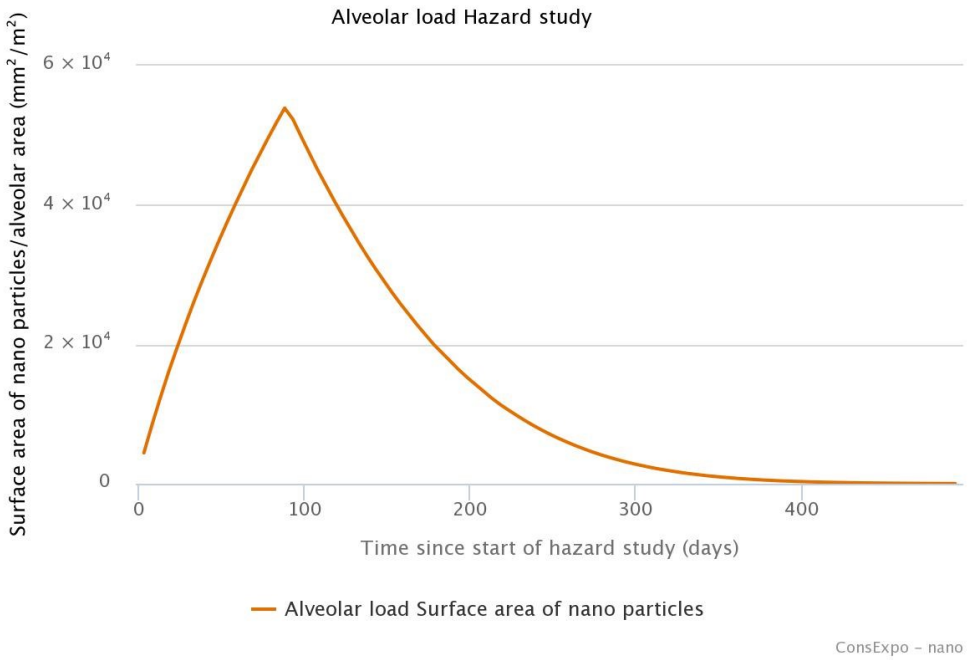

Figure 2 Estimated retained dose of TiO_2 in rat exposed for 13 weeks at concentration of 2.0 mg/m³ (settings experiment Bermudez et al.).

4.1 Human exposure

The human exposure (figure 1) is the result of two spray events in the one year that the exposure is evaluated.The first exposure event is assumed to be on day 0, where the deposited dose gives rise to an initial alveolar load. The retained dose in the alveoli decreases over time due to alveolar clearance until, 6 months later, a second painting event takes place. This event gives rise to another increase in the alveolar load. After this, the retained dose again declines. The maximum alveolar dose is almost 5000 mm^2/m^2 (in surface area of nanomaterial per unit surface area of the alveolar surface).

4.2 Hazard study

The retained dose in rat from the (Bermudez et al., 2006) study results from 91 days of inhalation exposure that leads to a deposited daily dose rate delivered to the alveoli that steadily builds up the retained alveolar dose. The alveolar load will, at the same time, be reduced by the clearance from the alveolar macrophages. After 91 days the maximum alveolar load is reached at a little bit above $5x10^4$ mm^2/m^2 (expressed as unit surface area per unit surface area of the alveoli.)

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4.3 Risk assessment

There are no clear procedures to follow when assessing the risk of inhalation of nanomaterials. It is, in this case study, for example uncertain to what measure of exposure adverse effects in the lung may most strongly be related to, i.e. whether this is the maximum dose reached at any specific time or rather the average load over a prolonged period. In this case study, it is observed that the human retained dose remains below the load that induced effects in the rat. Whether the margin is sufficient to assume that the product's use in this scenario can be considered safe can not be concluded on the basis of these findings alone. However, the ConsExpo nano evaluation provides support for a more informed decision.

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