eurofins | BioPharma Product Testing

RISK ASSESSMENT OF THE PRODUCT

REair ORIGINAL

Contract n: MW3PPH200036-02

Sponsor:

REair S.r.l.
Via Montenapoleone 10
20121 Milano (MI)
ITALY

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LIST OF TERMS

AEL= Accepted exposure level
MMAD = medium mass aerodynamic diameter
NOAEC = No Observed Adverse Effect Concentration
NOAEL = No Observed Adverse Effect Level
PPE = Personal Protective Equipment
RCR = Risk Characterization Ratio

BIBLIOGRAPHY

[1] E. Commission, “COMMISSION DELEGATED REGULATION (EU) 2020/217,” *Off. J. Eur. Communities*, vol. L44, no. 18/2/2020, pp. 1–14, 2019.

[2] E. Commission, “CA-Nov14-Doc.5.11 Subject: Substances of Concern – Proposed Human Health (Toxicology) Assessment Scheme for Authorisation of Biocidal Products,” 2014.

[3] H. J. Bremmer, H. J. Bremmer, I. R. Assessment, and C. Products, “ConsExpo Paint Products Fact Sheet,” no. 612810010, pp. 1–49, 2007.

[4] J. D. Te Biesebeek, “General Fact Sheet General default parameters for estimating consumer exposure-Updated version 2014.”

[5] European Commission-Joint Research Centre, “HEEG OPINION 17 Default human factor values for use in exposure assessments for biocidal products,” vol. 2013, no. d, p. 6, 2013.

[6] A. G. S. J.E. Delmaar, “ConsExpo Web Consumer Exposure models documentation,” 2016.

[7] European Chemicals Agency, “Biocides Human Health Exposure Methodology,” 2015.

[8] European Chemicals Agency, *Guidance on the Application of the CLP Criteria (v 5.0)*, no. 1272. 2017.

ASSESSMENT REPORT

1 SUMMARY OF THE PRODUCT ASSESSMENT

1.1 Administrative information

1.1.1 Identifier of the product

Identifier	Country
REair Original	Italy

1.1.2 Manufacturer(s) of the product

Name of manufacturer	REair S.r.l.

Address of manufacturer	P.le Principessa Clotilde, 6 – 20121 Milano
Location of manufacturing sites	P.le Principessa Clotilde, 6 – 20121 Milano

1.2 Product composition and formulation

Qualitative and quantitative information on the composition of the product

Common name	Chemical name	Function	CAS number	Content (%)
[redacted]	Titanium dioxide	pigment	[redacted]	[redacted]
[redacted]	Copolymer with pigment affinic groups	dispersant/wetting agent	[redacted]	[redacted]
[redacted]	Silicic acid, potassium salt	stabilizer/ ligand	[redacted]	[redacted]
[redacted]	Polydimethylsiloxane and auxiliary,(emulsion in water)	antifoam-emulsifier	[redacted]	[redacted]
[redacted]	water	solvent	[redacted]	[redacted]

1.2.1 Type of formulation

Liquid suspo - emulsion

1.3 Hazard and precautionary statements

Classification and labelling of the products of the family according to the Regulation (EC) 1272/2008

Classification	
Hazard category	-
Hazard statement	-
Labelling	
Signal words	-
Hazard statements	-
Precautionary statements	-
Note	the product is not classified according to the CLP regulation

1.4 Use(s)

1.4.1 Use description

Table 1. Use # 1 – name of the use

Application method(s)	Flayrsol
Application rate(s) and frequency	1.2 ml/sec 16.6 ml/m^2

Category(ies) of users	General public and Professionals
Pack sizes and packaging material	Polyethylene containers 200 ml

Table 2. Use # 2 – HVLP guns

Application method(s)	Airless HVLP high volume - low pressure gun (max 0.15 bar)
Application rate	1000 ml/h 16.6 ml/m^2
Category(ies) of users	Professionals
Pack sizes and packaging material	Polyethylene containers 1l – 5l – 25l

1.4.2 Use-specific instructions for use #1

The bottle is aimed to the wall and sprayed to cover the surface of interest. The product is aimed to be used indoor.

1.4.3 Use-specific risk mitigation measures for use #1

No specific mitigation measure is required

1.4.4 Use-specific instructions for use #2

The product is transferred into the gun reservoir by pouring it slowly. The gun is aimed to the wall and sprayed to cover the surface of interest. The product is aimed to be used indoor.

1.4.5 Use-specific risk mitigation measures for use #2

No specific mitigation measure is required

1.4.6 Where specific to the use #1 and #2, the particulars of likely direct or indirect effects, first aid instructions and emergency measures to protect the environment

No damage to the users is known. In case of need, the following safety measures should be taken: Inhalation: Take the subject to fresh air. If breathing stops, give artificial respiration. Consult immediately a doctor. Ingestion: See a doctor immediately. Induce vomiting only if directed by your doctor. Do not give anything by mouth if the subject is unconscious. Eyes and Skin: Wash with plenty of water. In case of persistent irritation, consult a doctor.

1.4.7 Where specific to the use, the instructions for safe disposal of the product and its packaging

Dispose according to the local laws.

1.4.8 Where specific to the use, the conditions of storage and shelf-life of the product under normal conditions of storage

The product can be stored for 24 months between 5 and 40°C

1.5 Packaging of the biocidal product

Type of packaging	Size/volume of the packaging	Material of the packaging	Type and material of closure(s)	Intended user (e.g. professional, non-professional)	Compatibility of the product with the proposed packaging materials (Yes/No)
Bottle	200 ml	Polyethylene	Polyethylene	general public	yes
Bottle and tank	1l – 5l – 25l	Polyethylene	Polyethylene	professional	yes

1.6 Substances of concern

The product components are the listed in the following table.

Common name	CAS number	Content (%)	Classification	Substance of concern
Titanium dioxide	[redacted]	[redacted]	Carc.2 by inhalation[1]	yes Band C[2] (full quantitative risk assessment, because systemic effects are foreseen)
Disperbuk-192	mixture	[redacted]	Not classified	no
CERRUS Silicic acid, potassium salt	[redacted]	[redacted]	H315 H318	yes Band B[2] (Only qualitative risk assessment because only local effects are foreseen)
SILOFOAM SE 47	mixture [redacted] [redacted]	[redacted]	H411 H412	no, it is not a substance of concern for human health
Water	[redacted]	[redacted]	Not classified	no

The classification of the components is not harmonised, so the substances of concern may change with time. A ‘substance of concern’ is a substance which has an inherent capacity to cause an adverse effect, immediately or in the more distant future, on humans, in particular vulnerable groups, animals or the environment and is present or is produced in a product in sufficient concentration to present risks of such an effect.
Since the product is not classified, it does not contain substances of concern, for this reason, the risk assessment was performed on the two substances that may pose a risk for human health, namely Titanium dioxide and Cerrus even if their amount was not sufficient to trigger the classification.
Titanium Dioxide will be subject to a full qualitative and quantitative risk assessment, whereas Cerrus will undergo only to a qualitative risk assessment because only local effects are foreseen.

1.7 Assessment of the product

1.7.1 Physical, chemical and technical properties of REair Original

Property	Results	Reference
Physical state at 20 °C and 101.3 kPa	liquid suspo-emulsion	SDS
Colour at 20 °C and 101.3 kPa	white	SDS
Odour at 20 °C and 101.3 kPa	odourless	Client declaration
pH	6-8	TDS
Relative density / bulk density	1.0 g/cm^3	SDS
Storage stability test – long term storage at ambient temperature	24 months	SDS

1.7.2 Physical hazards and respective characteristics

Property	Structural considerations
Explosives	none of the co-formulants are explosive
Flammable liquids	none of the co-formulants are flammable
Self-reactive substances and mixtures	there is no evidence that the product is self reactive
Pyrophoric liquids	none of the co-formulants are Pyrophoric
Substances and mixtures which in contact with water emit flammable gases	none of the co-formulants emit flammable gases in contact with water; in any case the product is an aqueous solution
Oxidising liquids	none of the co-formulants are oxidizing
Organic peroxides	none of the co-formulants are organic peroxides
Corrosive to metals	none of the co-formulants are corrosive to metals
Auto-ignition temperatures of products (liquids and gases)	all the co-formulants have very high auto-ignition temperatures

Conclusion on the physical hazards and respective characteristics of the product
Due to the characteristics of its co-formulants, the product does not create a physical hazard.

1.8 Risk assessment for human health

The product is not classified as dangerous according to CLP regulation (EC 1272/2008). In any case the sponsor decided to perform a test on skin irritation, to prove that the product is not irritant to the skin.

1.8.1 Assessment of effects on Human Health

Skin corrosion and irritation

Summary table of in vitro studies on skin corrosion/irritation			
Method,Guideline, GLP status, Reliability	Results	**Remarks** (e.g. major deviations)	Reference
OECD439 performed in GLP	Not irritant	no deviation	STULV20AA0398-1

Conclusion used in Risk Assessment – Skin corrosion and irritation	
Value/conclusion	NOT IRRITANT
Justification for the value/conclusion	the cell viability was > 90%
Classification of the product according to CLP and DSD	NOT CLASSIFIED

Eye irritation

Data waiving	
Information requirement	eye irritation
Justification	The product is not classified for eye irritation, so the test is not necessary

Respiratory tract irritation

Data waiving	
Information requirement	respiratory tract irritation
Justification	None of the co-formulant of the product are classified for respiratory tract irritation, so the test is not considered necessary

Skin sensitization

Data waiving	
Information requirement	skin sensitization
Justification	None of the co-formulant of the product are classified as skin sensitizer, so the test is not considered necessary

Acute toxicity

Titanium dioxide:
Acute oral toxicity: LD50 > 5000 mg/kg bw so no risk arises from the ingestion of titanium dioxide

Acute inhalation toxicity: LC50 > 6.82 mg/L (MMAD=1.55 µm) the concentration value is very high and the medium diameter of the particles is far below that of the normal use of the product.
Acute dermal toxicity: Titanium dioxide is not absorbed to any relevant extent through human skin, thus no toxic effects can be expected via the dermal route of exposure.[1]

Data waiving	
Information requirement	Acute toxicity by oral, inhalation and dermal route
Justification	None of the co-formulant of the product are classified for any kind of acute toxicity, so the tests are not considered necessary

1.8.2 Exposure assessment

The product is supposed to be used both from the general public and from the professional users. The product is supposed to be sprayed when in the room only the operator is present. The public will be allowed in the room once the product is dry.
For these reasons no risk of secondary exposure is foreseen for bystanders. Moreover the vapour pressures of the co-formulants identified as substances of concern (Titanium dioxide and Silicic acid, potassium salt) are very low and they can be considered as non-volatile (where 'volatile' is defined as compounds with vapour pressure > 0.1 Pa, 'non-volatile' < 0.01 Pa and 'slightly volatile' between 0.01and 0.1 Pa).

Summary table: relevant paths of human exposure							
Exposure path	Primary (direct) exposure			Secondary (indirect) exposure			
	Industrial use	Professional use	Non-professional use	Industrial use	Professional use	General public	Via food
Inhalation	No	Yes	Yes	No	No	No	No
Dermal	No	Yes	Yes	No	No	No	No
Oral	No	No	No	No	No	No	No

1.8.2.1 List of scenarios

The scenarios listed below are those referred to the use of the product.
General public will use ready to use products with an integrated spraying device. For this reason, for them, the only exposure scenario is that due to the spraying procedure.
On the other hand, Professionals will use pumping devices which will require a filling step. The exposure of professionals will be due both to the mixing and loading procedure, where the product is loaded into the spraying device, and to the spraying step.
A fourth exposure scenario is that relative to people staying in rooms where the product has been previously sprayed. It is possible that they might inhale the volatile components of the product. Since both the identified substances of concern are non-volatile, this risk is negligible and it will not be considered.

[1] All the acute toxicity data arise from the REACH dossier of Titanium Dioxide.

Summary table: scenarios			
Scenario number	**Scenario**	**Primary or secondary exposure Description of scenario**	**Exposed group**
1.	Application	**Primary exposure:** The product is sprayed on an indoor wall. During this step the product can come into contact with the skin of the user and may also be inhaled.	General public
2.	Mixing and loading	**Primary exposure:** The product is loaded into the spraying device. During this step the product can come into contact with the skin of the user and may also be inhaled. Since the user is a professional, he will be equipped with PPE such and gloves and facial mask. The first tier of the risk assessment will not take into account the use of PPE.	Professionals
3.	Application	**Primary exposure:** The product is sprayed on an indoor wall. During this step the product can come into contact with the skin of the user and may also be inhaled. Since the user is a professional, he will be equipped with PPE such and gloves and facial mask. The first tier of the risk assessment will not take into account the use of PPE.	Professionals
4.	Staying in the room after the product has been sprayed	**Secondary exposure:** The product sprayed on the surfaces may have volatile components that could be inhaled by bystanders staying in the room whose walls have been treated with the product under scrutiny. The two substances that might raise a concern have the following vapour pressures: Titanium dioxide: the study of vapour pressure determination was not conducted because the melting point was above 300°C. Silicic acid, potassium salt: the study of vapour pressure determination was not conducted because the melting point was above 300°C. The vapour pressure of the two substances are quite low, so the risk of exposure of bystanders is negligible, and this exposure scenario will not be investigated any further.	Bystanders

1.8.2.2 Industrial exposure

A consideration of Industrial exposure during manufacture of the biocidal products is not required as this is covered by other legislation..
The production cycle is performed in a closed system with controlled registration and the ingredients are dosed by an operator equipped with the necessary PPE.

1.8.2.3 General Public exposure

Scenario [1]

Description of Scenario 1 – Application – General public
The non-professional user aims the product can on to a wall and sprays all over it. The application of the product on indoor surfaces from general public is described by ConsExpo in the Paint Product Fact Sheet[3]. During spraying, an aerosol cloud of very small to small droplets is formed. The user can inhale these aerosol particles. To calculate the inhalation exposure to aerosol particles, the 'spray model' from ConsExpo is used for both spraying with a spray can and spraying using a compressor. The use of the product by general public is described by the model: "spray can". The ConsExpo **spray model** is developed on the basis of the results of experimental work and describes the indoor inhalation exposure to slightly evaporating or non-volatile compounds in droplets that are released from a spray can. For volatile compounds, the evaporation model is more appropriate, but the since the substances of concern inside the product are non-volatile, the spray model was used. The droplet size is an important parameter when estimating exposure via inhalation. Smaller drops fall at a lower speed and stay in the air for longer. The large droplets will quickly disappear from the air after being formed. To calculate the dermal exposure of the user during application, the 'constant rate' model from ConsExpo, is used for both spray applications.

The following table reports the values of the particle size distribution of 2 types of paints: Paint 1 (water based) and Paint 2 (solvent based)[3]: REair Original belongs to the first group. So the particle size is above 20 µm.

Application	**Content**	**Percentiles of the initial particle distribution [µm]**		
		D_p (0.10)	**D_p (0.50)**	**D_p (0.90)**
Surface spraying, aerosol cans				
Paint 1	Full Nearly empty	27 20	114 76	352 186
Paint 2	Full Nearly empty	11 10	39 37	88 101

Here below are listed the parameters used to calculate the exposure in the different scenarios, along with some comments on them.

	Default value	Source
Inhalation – exposure to spray – spraying		
Frequency	2 per year	ConsExpo web default
Spray duration	Default = 15 minutes.	A room has a default volume of 34 m^3 and a default height of 2,25 m[3]. The area of the ceiling is 15.1 m^2. Assuming a

		square room, it would be 3.89 m long. The total area of the 4 walls and the ceiling would be: [(3.89m x 2.25 m) x 4] +15.1m^2 = 50.1m^2. The product sprays 1.2 ml/sec and 16.6 ml/m^2. So to cover the entire room: 16.6 ml/m^2 x 50.1m^2 = 831,61 ml will be necessary. The spray duration will be 831,61 ml / 1.2 ml/sec = 693.01 sec = 11.6 minutes, so the default time of 15 minutes is acceptable[3].
Exposure duration	20 minutes	Default[3]
Weight fraction of the substance (titanium dioxide)	0.95%	See product composition
Room volume	34 m^3	Default[3]
Room height	2.25 m	Default[3]
Ventilation rate	1.5 per hour	Default[3]
Inhalation rate	1.49 m^3/h	Default value for an adult of 68.9 kg, performing a light exercise[4].
Mass generation rate	0.33 g/s	Default[3]
Airborne fraction	1	Default[3]
Density non volatile	1.5 g/cm^3	See ConsExpo Web defaults Exposure to spray – spraying model
Inhalation cut off diameter	15 µm	Default[3] The inhalation cut-off diameter is the measure for the diameter of the spray droplets that can be inhaled and reach the lower areas of the lungs (alveoli, bronchioles, bronchia). Particles larger than this diameter deposit in the higher parts of the respiratory tract and will be cleared via the gastro-intestinal tract, leading to oral exposure. The inhalation cut-off diameter is only an approximation of the complicated process of deposition of particles in the lung. In general, this value will be around 10-15 µm. The default value is set at 15 µm.
Aerosol diameter distribution type	Log-normal	Default[3]
Median diameter	30 µm	Default[3]
Arithmic coefficient of variation	0.8	Default[3]
Maximum diameter	90 µm	Default[3]
Absorption – fixed fraction	75%	No data are available, the value has been chosen as a worst case scenario

	Default value	Source
Dermal – exposure – direct product contact – constant rate		
Frequency	2 per year	See ConsExpo Web defaults Exposure to spray – spraying model
Exposed area	820 cm^2	Default values for adults hands[5] (at the moment no PPE is taken into account)
Weight fraction of the substance (titanium dioxide)	0.95%	See product composition

Contact rate	100 mg/min	Default[3]
Release duration	15 min	Default[3]
Absorption – fixed fraction	25%	Literature data indicates that titanium dioxide id not absorbed to any relevant extent through human skin. As a worst case scenario an adsorption of 25% was used.

The data below are the output of the ConsExpo web program which starting with the input data of the table above, produced the output values of inhalation and dermal exposure of the User.

Inhalation

Exposure model Exposure to spray - Spraying
Absorption model Fixed fraction

Mean event concentration 3.7 mg/m³
average air concentration on exposure event. Note: depends strongly on chosen exposure duration

Peak concentration (TWA 15 min) 4.4 mg/m³
peak concentration (TWA 15 min) is the 15 minute time weighted average of the air concentration. In case the exposure duration is less than 15 minutes, the mean event air concentration is given instead.

Mean concentration on day of exposure 5.1×10^{-2} mg/m³
average air concentration over the day (accounts for the number of events on one day)

Year average concentration 2.8×10^{-4} mg/m³
mean daily air concentration averaged over a year

External event dose 2.7×10^{-2} mg/kg bw
the amount that can potentially be absorbed per kg body weight during one event

External dose on day of exposure 2.7×10^{-2} mg/kg bw
the amount that can potentially be absorbed per kg body weight during one day

Internal event dose 2.0×10^{-2} mg/kg bw
absorbed dose per kg body weight during one exposure event

Internal dose on day of exposure 2.0×10^{-2} mg/kg bw/day
absorbed dose per kg body weight during one day. Note: these can be higher than the 'event dose' for exposure frequencies larger than 1 per day.

Internal year average dose 1.1×10^{-4} mg/kg bw/day
daily absorbed dose per kg body weight averaged over a year.

Dermal

Exposure model Direct product contact - Constant rate
Absorption model Fixed fraction

Dermal load	1.7×10^{-2}	mg/cm²
amount per cm² on the skin		
External event dose	2.1×10^{-1}	mg/kg bw
the amount that can potentially be absorbed per kg body weight during one event		
External dose on day of exposure	2.1×10^{-1}	mg/kg bw
the amount that can potentially be absorbed per kg body weight during one day		
Internal event dose	5.2×10^{-2}	mg/kg bw
absorbed dose per kg body weight during one exposure event		
Internal dose on day of exposure	5.2×10^{-2}	mg/kg bw/day
absorbed dose per kg body weight during one day. Note: these can be higher than the 'event dose' for exposure frequencies larger than 1 per day.		
Internal year average dose	2.8×10^{-4}	mg/kg bw/day
daily absorbed dose per kg body weight averaged over a year.		

Integrated

Internal event dose	7.2×10^{-2}	mg/kg bw
absorbed dose per kg body weight during one exposure event		
Internal dose on day of exposure	7.2×10^{-2}	mg/kg bw/day
absorbed dose per kg body weight during one day. Note: these can be higher than the 'event dose' for exposure frequencies larger than 1 per day.		
Internal year average dose	3.9×10^{-4}	mg/kg bw/day
daily absorbed dose per kg body weight averaged over a year.		

Summary table: estimated exposure from General public uses (systemic values)					
Exposure scenario	Tier/PPE	Estimated inhalation uptake	Estimated dermal uptake	Estimated oral uptake	Estimated total uptake
Scenario [1]	Tier 1 no refinement was applied	0.020 mg/kg bw d	0.052 mg/kg bw d	the exposure scenario does not assume any oral uptake	0.072 mg/kg bw d

1.8.2.4 Professional exposure

Scenario [2]

Description of Scenario 2 – Mixing and Loading (professional users)
A professional user using a spraying gun is supposed to load it just before use. The loading of the product in the spraying device, immediately before use, may lead to inhalation and dermal exposure. Several models can be used to describe the user exposure. ConsExpo fact sheets were selected because they offer reliable models for general public, which can be adapted to professional users as well. Inhalation exposure can occur if volatile compounds evaporate during the loading process, and since the user stays in the vicinity of the evaporating compound and it is assumed that the user is present in a 'personal volume' instead of a room volume. As default model to describe the inhalation exposure from mixing and loading the 'exposure to vapour: evaporation model' is selected[6][3]. Further, there could be dermal exposure due to spillage. To calculate the exposure of the user during mixing and loading liquid, the 'instant application' model is used for dermal exposure[6][3]. The tool used for the estimation of the exposure during the Scenario 2 – Mixing and Loading is ConsExpo Web version 1.0.6, released in February 2019, supported by the Paint Product Fact Sheet.

The following table reports the parameters using during the calculations and the reasons for such choices:

Inhalation exposure

	Default value	Source
Inhalation–exposure to vapour–evaporation		
Frequency	1 per day	Daily exposure for professional users. See ECHA default values for the exposure and risk assessment process (human exposure for professionals), whenever no better (underpinned) data are available. Data referred to Biocides PT7 (film preservatives)[7]
Exposure duration	1 hour	Total duration mixing and loading per day (default)[7]
Product amount	6 kg	The system sprays 1000 ml/h. According to the table on PT7 of Biocides human health exposure methodology, a professional sprays for 6 hours a day, for a total of 6 litres of product, so approximately 6 kg.
Weight fraction of the substance (titanium dioxide)	0.95%	See product composition

Room volume	1 m^3	'Room volume' is interpreted here as 'personal space': a small volume of 1 m^3 around the user. A small volume around the user is relevant for the inhalation exposure of the user, for the short use duration in which the treatment takes place[3].
Ventilation rate	0.6 per hour	The ventilation rate for an unspecified room (i.e. 0.6 hr^{-1}) is used, because no information is available on the ventilation rate near the user[3].
Inhalation rate	1.49 m^3/h	Default value for an adult of 68.9 kg performing a light exercise[4].
Vapour pressure of Titanium dioxide	0.01 Pa	Extrapolated value for non volatile substances.
Application temperature	20°C	Room temperature
Molecular weight of Titanium Dioxide	79.88 g/mol	
Mass transfer coefficient	18.3 m/hr	Thibodeaux's method
Release area mode - constant		
Release area	78.5 cm^2	Loading area of a reservoir of a spraying gun with a diameter of 10 cm.
Emission duration	1 hour	The emission in the vapour phase is supposed to last throughout all the loading procedure
Absorption – fixed fraction	75%	No data are available, the value has been chosen as a worst case scenario

Dermal exposure

Dermal exposure could occur due to spillages around the opening of the paint can and spatters during the loading. Information about dermal exposure of paint products during the mixing and loading process was not found. The contamination from emptying different volume containers with wide necks, loaded with liquids, varies from 0.01 to 0.05 ml per operation, depending on the container size.

The dermal exposure of hands and forearms results in a range from 0 to 3.2 mg/event (averaged over four events) and in a worst case single event of 12.8 mg/event.

Based on the information above the default value for the quantity of product that ends up to the skin is set at 50 mg/event (value derived from the PSD; 0.05 ml per operation = 50 mg, if the density of the liquid is 1 g/cm^3).

All these data suggest a minimal spillage of the product on the hands during the mixing and loading procedure. It is assumed that a professional consumes 6 litres of product per day. Using 1 litre bottles he will have to reload the spraying equipment 6 times: leading to 50 mg x 6 times = 300 mg.

It is also assumed that the professional user is not wearing gloves.

This is the worst case scenario possible.

	Default value	Source
Dermal – exposure – instant application		
Frequency	1 per day	Daily exposure for professional users. See ECHA default values for the exposure and risk assessment process (human exposure for professionals), whenever no better (underpinned) data are available. Data referred to Biocides PT7 (film preservatives)[7]
Exposed area	820 cm^2	Default values for adults hands[5] (at the moment no PPE is taken into account)
Product amount	300 mg	The system sprays 1000 ml/h. According to the table on PT7 of Biocides human health exposure methodology, a professional sprays for 6 hours a day, for a total of 6 litres of product. Using 1 litre bottles he will have to reload the spraying equipment 6 times: leading to 50 mg x 6 times = 300 mg of product on his hands.
Weight fraction of the substance (titanium dioxide)	0.95%	See product composition
Absorption – fixed fraction	25%	Literature data indicates that titanium dioxide id not absorbed to any relevant extent through human skin. As a worst case scenario an adsorption of 25% was used.

The data below are the output of the ConsExpo web program which starting with the input data of the table above, produced the output values of inhalation and dermal exposure of the User.

Inhalation

Exposure model Exposure to vapour - Evaporation
Absorption model Fixed fraction

Mean event concentration	1.9×10^{-2}	mg/m³

average air concentration on exposure event. Note: depends strongly on chosen exposure duration

Peak concentration (TWA 15 min)	3.0×10^{-2}	mg/m³

peak concentration (TWA 15 min) is the 15 minute time weighted average of the air concentration. In case the exposure duration is less than 15 minutes, the mean event air concentration is given instead.

Mean concentration on day of exposure	7.8×10^{-4}	mg/m³

average air concentration over the day (accounts for the number of events on one day)

Year average concentration	7.8×10^{-4}	mg/m³

mean daily air concentration averaged over a year

External event dose	4.0×10^{-4}	mg/kg bw

the amount that can potentially be absorbed per kg body weight during one event

External dose on day of exposure	4.0×10^{-4}	mg/kg bw

the amount that can potentially be absorbed per kg body weight during one day

Internal event dose	3.0×10^{-4}	mg/kg bw

absorbed dose per kg body weight during one exposure event

Internal dose on day of exposure	3.0×10^{-4}	mg/kg bw/day

absorbed dose per kg body weight during one day. Note: these can be higher than the 'event dose' for exposure frequencies larger than 1 per day.

Internal year average dose	3.0×10^{-4}	mg/kg bw/day

daily absorbed dose per kg body weight averaged over a year.

Dermal

Exposure model Direct product contact - Instant application
Absorption model Fixed fraction

Dermal load	3.5×10^{-3}	mg/cm²
amount per cm² on the skin		
External event dose	4.1×10^{-2}	mg/kg bw
the amount that can potentially be absorbed per kg body weight during one event		
External dose on day of exposure	4.1×10^{-2}	mg/kg bw
the amount that can potentially be absorbed per kg body weight during one day		
Internal event dose	1.0×10^{-2}	mg/kg bw
absorbed dose per kg body weight during one exposure event		
Internal dose on day of exposure	1.0×10^{-2}	mg/kg bw/day
absorbed dose per kg body weight during one day. Note: these can be higher than the 'event dose' for exposure frequencies larger than 1 per day.		
Internal year average dose	1.0×10^{-2}	mg/kg bw/day
daily absorbed dose per kg body weight averaged over a year.		

Integrated

Internal event dose	1.1×10^{-2}	mg/kg bw
absorbed dose per kg body weight during one exposure event		
Internal dose on day of exposure	1.1×10^{-2}	mg/kg bw/day
absorbed dose per kg body weight during one day. Note: these can be higher than the 'event dose' for exposure frequencies larger than 1 per day.		
Internal year average dose	1.1×10^{-2}	mg/kg bw/day
daily absorbed dose per kg body weight averaged over a year.		

Scenario [3]

Description of Scenario 3 – Application – (professional users)
Once the professional user has loaded the spraying gun, he aims it to the wall to cover it with the product. The application of the product on indoor surfaces from Professionals is not described by ConsExpo, but the Paint Product Fact Sheet[3] can be adapted to describe the scenario of professional users. As a first tier PPE will not be taken into account. Many of the considerations performed in scenario 1 are applicable to scenario 3.

	Default value	Source
Inhalation – exposure to spray – spraying		

Frequency	1 per day	Daily exposure for professional users. See ECHA default values for the exposure and risk assessment process (human exposure for professionals), whenever no better (underpinned) data are available. Data referred to Biocides PT7 (film preservatives)[7]
Spray duration	6 hours	Total duration of spraying per day (default)[7]
Exposure duration	6 hours	(default)[7]
Weight fraction of the substance (titanium dioxide)	0.95%	See product composition
Room volume	34 m^3	Default[3]
Room height	2.25 m	Default[3]
Ventilation rate	1.5 per hour	Default[3]
Inhalation rate	1.49 m^3/h	Default value for an adult of 68.9 kg performing a light exercise[4].
Mass generation rate	0.33 g/s	Default[3]
Airborne fraction	1	Default[3]
Density non volatile	1.5 g/cm^3	See ConsExpo Web defaults Exposure to spray – spraying model
Inhalation cut off diameter	15 µm	Default[3]
Aerosol diameter distribution type	Log-normal	Default[3]
Median diameter	30 µm	Default[3]
Arithmic coefficient of variation	0.8	Default[3]
Maximum diameter	90 µm	Default[3]
Absorption – fixed fraction	75%	No data are available, the value has been chosen as a worst case scenario

	Default value	Source
Dermal – exposure – direct product contact – constant rate		
Frequency	1 per day	Daily exposure for professional users. See ECHA default values for the exposure and risk assessment process (human exposure for professionals), whenever no better (underpinned) data are available. Data referred to Biocides PT7 (film preservatives)[7]
Exposed area	820 cm^2	Default values for adults hands[5] (at the moment no PPE is taken into account)
Weight fraction of the substance (titanium dioxide)	0.95%	See product composition
Contact rate	100 mg/min	Default[3]
Release duration	6 hours	Total duration of spraying per day (default)[7]
Absorption – fixed fraction	25%	Literature data indicates that titanium dioxide id not absorbed to any relevant extent through human skin. As a worst case scenario an adsorption of 25% was used.

The data below are the output of the ConsExpo web program which starting with the input data of the table above, produced the output values of inhalation and dermal exposure of the User.

Inhalation

Exposure model Exposure to spray - Spraying
Absorption model Fixed fraction

Mean event concentration	6.7	mg/m³
average air concentration on exposure event. Note: depends strongly on chosen exposure duration		
Peak concentration (TWA 15 min)	6.9	mg/m³
peak concentration (TWA 15 min) is the 15 minute time weighted average of the air concentration. In case the exposure duration is less than 15 minutes, the mean event air concentration is given instead.		
Mean concentration on day of exposure	1.7	mg/m³
average air concentration over the day (accounts for the number of events on one day)		
Year average concentration	1.7	mg/m³
mean daily air concentration averaged over a year		
External event dose	8.8×10^{-1}	mg/kg bw
the amount that can potentially be absorbed per kg body weight during one event		
External dose on day of exposure	8.8×10^{-1}	mg/kg bw
the amount that can potentially be absorbed per kg body weight during one day		
Internal event dose	6.6×10^{-1}	mg/kg bw
absorbed dose per kg body weight during one exposure event		
Internal dose on day of exposure	6.6×10^{-1}	mg/kg bw/day
absorbed dose per kg body weight during one day. Note: these can be higher than the 'event dose' for exposure frequencies larger than 1 per day.		
Internal year average dose	6.6×10^{-1}	mg/kg bw/day
daily absorbed dose per kg body weight averaged over a year.		

Dermal

Exposure model Direct product contact - Constant rate
Absorption model Fixed fraction

Dermal load	4.2×10^{-1}	mg/cm²
amount per cm² on the skin		
External event dose	5.0	mg/kg bw
the amount that can potentially be absorbed per kg body weight during one event		
External dose on day of exposure	5.0	mg/kg bw
the amount that can potentially be absorbed per kg body weight during one day		
Internal event dose	1.2	mg/kg bw
absorbed dose per kg body weight during one exposure event		
Internal dose on day of exposure	1.2	mg/kg bw/day
absorbed dose per kg body weight during one day. Note: these can be higher than the 'event dose' for exposure frequencies larger than 1 per day.		
Internal year average dose	1.2	mg/kg bw/day
daily absorbed dose per kg body weight averaged over a year.		

Integrated

Internal event dose	1.9	mg/kg bw
absorbed dose per kg body weight during one exposure event		
Internal dose on day of exposure	1.9	mg/kg bw/day
absorbed dose per kg body weight during one day. Note: these can be higher than the 'event dose' for exposure frequencies larger than 1 per day.		
Internal year average dose	1.9	mg/kg bw/day
daily absorbed dose per kg body weight averaged over a year.		

The systemic exposure of a professional user is summarised in the following table. It accounts for the two exposure scenarios of mixing and loading and of application

Summary table: systemic exposure associated with professional use				
Scenarios combined	Estimated inhalation uptake	Estimated dermal uptake	Estimated oral uptake	Estimated total uptake
Scenario [2] Mixing and loading	0.0003 mg/kg bw day	0.01 mg/kg bw day	the exposure scenario does not assume any oral uptake	0.01 mg/kg bw day
Scenario [3] Application	0.66 mg/kg bw day	1.2 mg/kg bw day	the exposure scenario does not assume any oral uptake	1.86 mg/kg bw day

1.8.2.5 Summary of exposure assessment

The table below summarises the total systemic exposure arising from each of the three exposure scenarios. All the data are obtained as a first tier and no PPE has been used to perform the calculations.

Scenarios and values to be used in risk assessment			
Scenario number	Exposed group	Tier/PPE	Estimated total uptake
1. Application	General public	1 no PPE	0.072 mg/kg bw day
2. Mixing and Loading	Professional users	1 no PPE	0.01 mg/kg bw day
3. Application	Professional users	1 no PPE	1.86 mg/kg bw day

The table below summarises the total systemic exposure arising from each of the three exposure scenarios and compares them with the no adverse effects limits derived by a long term study (90 days).[2] The exposure of the user in each scenario is well below the NOAEL. The NOAEL was used to derive the AEL. A precautionary assessment factor of 100 was used to account for the intra species (10) and interspecies corrections (10). So the AEL = NOAEL/100 =10 mg/kg bw/d.

Systemic effects

Task/ Scenario	Tier	Systemic NOAEL mg/kg bw/d (derived by 90 days study)	Systemic AEL mg/kg bw/d (derived AF=100)	Estimated uptake mg/kg bw/d	RCR= Estimated uptake/ AEL	Acceptable RCR <1 yes RCR > 1 no
1. Application	1	1000	10	0.072	0.0072	yes
2. Mixing and Loading	1	1000	10	0.01	0,001	yes
3. Application	1	1000	10	1.86	0.186	yes

The table below combines the two scenarios for the professional users (mixing and loading and application). Also in this case the exposure is well below the AEL.

Combined scenarios

Scenarios combined	Tier	Systemic AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	RCR= Estimated uptake/ AEL	Acceptable RCR <1 yes RCR > 1 no
1	1	10	0.072	0.0072	yes
2 and 3	1	10	1.87	0.187	yes

[2] Data taken from the REACH dossier of titanium dioxide.

1.8.2.6 Local effects (titanium dioxide)

The table below reports, for titanium dioxide, the data of the local exposure for the 3 scenarios examined both for inhalation and dermal routes. The table also reports the NOAEC values for inhalation and dermal local effects. The exposure is acceptable when the % ratio between exposure and NOAEC values is below 100.

Task/ Scenario	Tier	Inhalation Local exposure mg/m^3	dermal Local exposure mg/cm^2	NOAEC inhalation mg/m^3	Exposure/ NOAEC% Acceptable (yes/no)	NOAEC dermal mg/cm^2	Exposure/ NOAEC Acceptable (yes/no)
1. Application	1	3.7	0.017	9.6	38.54% (yes)	no adverse effect	yes
2. Mixing and Loading	1	0.019	0,0035	9.6	0.20% (yes)	no adverse effect	yes
3. Application	1	6.7	0.42	9.6	69.80% yes	no adverse effect	yes

The data show that as far as the inhalation is concerned, all scenarios are below the NOAEC.
No adverse effects are known for the dermal exposure. The exposures due to scenarios 1, 2 and 3 are quite low.

1.8.2.7 Local effects (silicic acid, potassium salt)

The raw material CERRUS is contained in the product at a concentration of 0.9%. The raw material contains at most 40% of Silicic acid, potassium salt. So the product contains at maximum 0.36% of Silicic acid, potassium salt. The presence of such a small amount of a skin irritating substance is not sufficient to trigger the classification H315 for the whole product[8]. The same holds for the eye irritation. For this reasons this co-formulant does not pose any risk for human health.

1.8.2.8 Conclusions

Three different scenarios have been evaluated.
The first describes the exposure of a non professional user spraying an indoor wall. Both the local and systemic effects do not raise any concern since the exposure is well below the adverse effect concentrations.
Local effects are not critical since the data on the dermal exposure clearly states that no adverse effect was evident, and that there is no indication of systemic adsorption through the skin[3].
Inhalation during spraying is not considered critical from a local point of view because the exposure is well below the NOAEC. Moreover the dimension of the particles sprayed is well above the inhalation cut off.
Systemic effect were considered assuming an adsorption of 75% for inhalation and a worst case scenario of 25% for the dermal route (no adsorption was evident). In any case the total systemic exposure was below the AEC values.
All the exposures have been calculated considering the possible worst case scenarios and assuming no PPE was used.

The same considerations apply to scenario 2 and 3 which describe the exposure of professional users.

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[3] See REACH dossier on Titanium dioxide

In its scientific opinion of 14 September 2017 on the substance titanium dioxide, RAC proposed to classify that substance as carcinogen category 2 by inhalation. The recent XIV ATP of CLP[1] gives some rules on mixtures containing titanium dioxide, namely: The classification as a carcinogen by inhalation applies only to mixtures in powder form containing 1 % or more of titanium dioxide which is in the form of or incorporated in particles with aerodynamic diameter ≤ 10 µm.
The mixture REair Original is not in the powder form, in any case the amount of titanium dioxide is below 1% (0.95%) and the MMAD of the sprayed particles is > 10 µm (it is expected to be around 20 µm in the worst case scenario), so the provisions on the labelling as Carc.2 do not apply.

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