



CHEMICAL SAFETY REPORT

Substance Name: [palladium dihydroxide](#)

EC Number: 235-219-2

CAS Number: 12135-22-7

Registrant's Identity:



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Part A



1. SUMMARY OF RISK MANAGEMENT MEASURES

The risk management measures for all Exposure Scenarios are described in Chapters 9 and 10 of part B of this CSR.

The above part A element applies to all uses



2. DECLARATION THAT RISK MANAGEMENT MEASURES ARE IMPLEMENTED

Each EU manufacturer and importer, having decided to mandate the Lead Registrant to submit this CSR on his behalf, endorses the declaration that he implements those risk management measures described in Part B, Chapter 9+10 of this document, that are relevant to his manufacture or import and own uses. Registrants that submit their own Part A are excluded from the afore-mentioned endorsement.

The above part A element applies to all uses



3. DECLARATION THAT RISK MANAGEMENT MEASURES ARE COMMUNICATED

Each EU manufacturer, importer and Only Representative having decided to mandate the Lead Registrant to submit this CSR on his behalf endorses the declaration that he communicates to distributors and the downstream users those risk management measures that are relevant for their uses as described in Part B, Section 9+10 of this document. Registrants that submit their own Part A are excluded from the afore-mentioned endorsement.

The above part A element applies to all uses



Part B



1. IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

1.1. Name and other identifiers of the substance

The substance [palladium dihydroxide](#) is a mono-constituent substance (inorganic) having the following characteristics and physical-chemical properties (see the IUCLID dataset for further details).

Table 1.1. Substance identity

EC number:	235-219-2
EC name:	palladium dihydroxide
CAS number (EC inventory):	12135-22-7
CAS number:	12135-22-7
IUPAC name:	palladium(2+) dihydroxide
Synonyms:	Palladium hydroxide (Pd(OH) ₂)
Molecular formula:	H ₂ O ₂ Pd
Molecular weight range:	140.435

Figure 1.1. 12135-22-7-V2.jpeg



1.2. Composition of the substance

Overall information on composition:

Composition	Related composition(s)
Palladium dihydroxide (legal entity composition of the substance)	
Palladium dihydroxide (boundary composition of the substance)	

Name: Palladium dihydroxide

(legal entity composition of the substance)

State/form: solid and powder

Degree of purity: % (w/w)

Description: Mono-constituent substance

Table 1.2. Constituents (Palladium dihydroxide)



Constituent	Typical concentration	Concentration range	Remarks
palladium dihydroxide EC no.:	% (w/w)	% (w/w)	

Table 1.3. Impurities (Palladium dihydroxide)

Constituent	Typical concentration	Concentration range	Remarks
water EC no.:	% (w/w)	% (w/w)	
sodium carbonate EC no.:	% (w/w)	% (w/w)	
Impurities EC no.:	ppm	% (w/w)	

Name: Palladium dihydroxide

(boundary composition of the substance)

State/form: solid and powder

Degree of purity: ≥ 85 - ≤ 100 % (w/w)

Description: Mono-constituent substance

Table 1.4. Constituents (Palladium dihydroxide)

Constituent	Typical concentration	Concentration range	Remarks
palladium dihydroxide EC no.:	91 % (w/w)	≥ 85 - ≤ 100 % (w/w)	

Table 1.5. Impurities (Palladium dihydroxide)

Constituent	Typical concentration	Concentration range	Remarks
water EC no.:	7 % (w/w)	≥ 0 - ≤ 15 % (w/w)	
sodium carbonate EC no.:	2 % (w/w)	≥ 0 - ≤ 2.5 % (w/w)	
Impurities EC no.:	300 ppm	≥ 0 - ≤ 1 % (w/w)	

1.3. Information on linked categories

None

1.4. Physicochemical properties

Table 1.6. Physicochemical properties

Property	Value used for CSA / Discussion	Description of key information
Physical state	<p>solid at 20°C and 101.3 kPa</p> <p>Walker and White (2011) is a GLP compliant, guideline experimental study. The statement on appearance is taken from a study on physico-chemical properties of this material, and is adequate for assessment as the key study for this endpoint. Palladium dihydroxide is a brown solid.</p> <p>Testing has also been conducted on a sample of 'palladium monoxide (hydrate)'. Further assessment of the substance identity of the test item indicated that based on the analytical data this sample was the</p>	Palladium dihydroxide is a brown solid.



	<p>same substance as palladium dihydroxide. Studies conducted on the sample of 'palladium monoxide (hydrate)' are therefore included in the dossier for palladium dihydroxide. The statement on appearance and physical state is taken from a GLP compliant, guideline experimental study for palladium monoxide (hydrate). The statement on appearance is taken from a study on physico-chemical properties of the material, and is adequate for assessment as the key study for this endpoint (O'Connor and Woolley 2011). Palladium monoxide (hydrate) is a fine black powder.</p>	
Melting / freezing point	<p>450°C at 101.3 kPa</p> <p>Walker and White (2011) is a GLP compliant, guideline study which is considered suitable for use as the key study for this endpoint. Palladium dihydroxide decomposed at 60°C with no definitive signs of melting below 450°C.</p> <p>Testing has also been conducted on a sample of 'palladium monoxide (hydrate)'. Further assessment of the substance identity of the test item indicated that based on the analytical data this sample was the same substance as palladium dihydroxide. Studies conducted on the sample of 'palladium monoxide (hydrate)' are therefore included in the dossier for palladium dihydroxide. O'Connor and Woolley (2011) is a GLP compliant, guideline study considered suitable for use as the key study for this endpoint. The melting point of palladium monoxide (hydrated solid) is > 450°C.</p>	<p>Palladium dihydroxide decomposed at 60°C with no definitive signs of melting below 450°C.</p>
Relative density	<p>3.44 at 20°C</p> <p>Potthoff (2011) is a guideline study which is considered suitable for use as the key study for this endpoint. The density of palladium hydroxide is 3.44 - 3.46 g/cm³ at 25°C.</p>	<p>The density of palladium hydroxide is 3.44 - 3.46 g/cm³ at 25°C.</p>
Granulometry	<p>Potthoff (2012) is a non-GLP, guideline experimental study, and is suitable for use as the key study for this endpoint. The average 10th, 50th and 90th percentile particle sizes for palladium dihydroxide were 0.27, 0.67 and 12.1 µm, respectively.</p>	<p>The average 10th, 50th and 90th percentile particle sizes for palladium dihydroxide were 0.27, 0.67 and 12.1 µm, respectively. The average specific surface area was determined as 133 ± 1.5 m²/g.</p>



	<p>The average specific surface area was determined as 133 ± 1.5 m²/g.</p> <p>Walker and White (2011) is a GLP compliant, guideline study providing a screening assessment of particle size for palladium dihydroxide. The proportion of palladium dihydroxide < 100 µm was 13.1 %.</p> <p>Testing has also been conducted on a sample of 'palladium monoxide (hydrate)'. Further assessment of the substance identity of the test item indicated that based on the analytical data this sample was the same substance as palladium dihydroxide. Studies conducted on the sample of 'palladium monoxide (hydrate)' are therefore included in the dossier for palladium dihydroxide. The particle size distribution of palladium monoxide (hydrate) was measured using Microtrac X-100 as part of a transformation / dissolution study (Skeaff and Beaudoin 2012). The results are considered to be suitable for use for this endpoint. The particle size distribution of palladium monoxide (hydrate) was determined and showed 50% of particles <62.3 µm.</p> <p>Specific surface area was determine using a Micromeritics Flowsorb II BET gas adsorption desorption technique. Specific surface area for palladium monoxide (hydrate) was determined to be 0.93 m²/g (calculated from particle size) and 7.93 m²/g (measured by BET).</p> <p>A screening assessment of particle size was conducted for a sample of palladium monoxide (hydrate) in a GLP compliant, guideline study (O'Connor and Woolley 2011). The proportion of palladium monoxide (hydrated solid) < 100 µm is 26.8%</p> <p>The dustiness of palladium dihydroxide was tested in a modified Heubach procedure according to the guideline DIN 55992-1:2006 (Selck and Parr 2011). The study is non-GLP, but follows a standard guideline and is considered to be reliable. The total dustiness of palladium dihydroxide was determined to be 138.92 mg/g. The inhalable fraction was 83.16 mg/g, the thoracic fraction was 14.97 mg/g and the respirable fraction was 3.16 mg/g. The Mass Median Aerodynamic Diameter (MMAD) was 29.77 µm with Geometric Standard Deviation of 2.13 µm.</p>	
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Water solubility	<p>0.13µg/L at 22.1°C</p> <p>Skeaff and Beaudoin (2012) is a non-GLP, guideline transformation / dissolution study and is suitable for use as a key study for this endpoint. In the 24-hour scoping tests, palladium hydroxide was at or below analytical limits, with net concentration changes being 0.1 and 0.0 µg/L for pH 6 and pH 8 respectively. The definitive test was performed at pH 6. The T/D data from the definitive test show that net concentration changes for palladium dihydroxide were 0.01, 0.21 µg/L and 0.4 µg/L after 7 days for 1, 10 and 100 mg palladium dihydroxide loadings, respectively. After 28 days, at a loading rate of 1 mg/L, the concentration was 0.13 µg/L.</p> <p>Testing has also been conducted on a sample of 'palladium monoxide (hydrate)'. Further assessment of the substance identity of the test item indicated that based on the analytical data this sample was the same substance as palladium dihydroxide. Studies conducted on the sample of 'palladium monoxide (hydrate)' are therefore included in the dossier for palladium dihydroxide. Skeaff and Beaudoin (2012) is a non-GLP, guideline transformation / dissolution study conducted with palladium monoxide (hydrate). The study is considered to be suitable for use as the key study for this endpoint. In the definitive T/D test performed with 'palladium monoxide (hydrate)', performed at pH 6, the net concentration changes for 'palladium monoxide (hydrate)' were <LOQ (0.1 µg/L), 8 µg/L and 98.9 µg/L, after 7 days at loading rates of 1, 10 and 100 mg/L, respectively. After 28 days, at a loading rate of 1 mg/L, measured palladium concentrations were <LOQ (0.1 µg/L).</p> <p>Water solubility testing was also conducted with palladium monoxide (hydrate) in a GLP compliant, guideline study (O'Connor and Woolley 2011). The study determined that the concentration of palladium monoxide (hydrate) in solution was less than 5.0×10^{-5}g/L of palladium at $20.0 \pm 0.5^\circ\text{C}$. This was equivalent to a palladium monoxide solubility of less than 6.6×10^{-5}g/l of solution at $20.0 \pm 0.5^\circ\text{C}$.</p>	<p>In the definitive T/D tests, performed at pH 6, the net concentration changes for palladium dihydroxide were 0.01, 0.21 µg/L and 0.4 µg/L after 7 days for 1, 10 and 100 mg palladium dihydroxide loadings, respectively. After 28 days, at a loading rate of 1 mg/L, the concentration was 0.13 µg/L. In a second test with a sample considered to be equivalent to palladium dihydroxide results were < LOQ (0.1 µg/L), 8 µg/L and 98.9 µg/L, after 7 days at loading rates of 1, 10 and 100 mg/L, respectively. After 28 days, at a loading rate of 1 mg/L, measured palladium concentrations were <LOQ (0.1 µg/L).</p>



<p>Autoflammability / self-ignition temperature</p>	<p>Walker and White (2011) is a GLP compliant, guideline study considered suitable for use as the key study for this endpoint. Palladium dihydroxide showed no signs of self-ignition or self heating over the duration of the test.</p> <p>Testing has also been conducted on a sample of 'palladium monoxide (hydrate)'. Further assessment of the substance identity of the test item indicated that based on the analytical data this sample was the same substance as palladium dihydroxide. Studies conducted on the sample of 'palladium monoxide (hydrate)' are therefore included in the dossier for palladium dihydroxide. O'Connor and Woolley (2011) is a GLP compliant, guideline study. Palladium monoxide (hydrate) showed no signs of self-ignition or self-heating in a N.4 (Modified method) Self Heating Substances test. A negative result was obtained.</p>	<p>Palladium dihydroxide showed no signs of self-ignition or self heating over the duration of the test.</p>
<p>Flammability</p>	<p>non flammable</p> <p>Walker and White (2011) is a GLP compliant, guideline study considered suitable for use as the key study for this endpoint. Palladium dihydroxide is not classified as a readily combustible solid under Division 4.1 as it failed to ignite in the preliminary screening test.</p>	<p>Palladium dihydroxide is not classified as a readily combustible solid under Division 4.1 as it failed to ignite in the preliminary screening test.</p>
<p>Oxidising properties</p>	<p>oxidising</p>	<p>Palladium dihydroxide is tested for oxidising properties using UN-Test O.1. Comparing the mean burning times of the sample mixtures with cellulose (t1 and t2) with the mean burning time of the reference mixture (R1), t1 or t2 are <R1. Therefore, it is concluded that palladium dihydroxide fulfils the classification criteria of Division 5.1 "Oxidizing substances", Packing group III, according to the Transport classification or hazard class 'oxidising solids', category 3, according to CLP.</p>

Data waiving

Information requirement: Boiling point



Reason: study scientifically not necessary / other information available

Justification: the study does not need to be conducted because the substance is a solid which decomposes before boiling [study scientifically not necessary / other information available]

Information requirement: Vapour pressure

Reason: study scientifically not necessary / other information available

Justification: the study does not need to be conducted because the melting point is above 300°C [study scientifically not necessary / other information available]

Information requirement: Partition coefficient n-octanol/water (log value)

Reason: study technically not feasible

Justification: the study does not need to be conducted because the substance is inorganic [study technically not feasible]

Information requirement: Surface tension

Reason: study scientifically not necessary / other information available

Justification: the study does not need to be conducted because based on structure, surface activity is not expected or cannot be predicted [study scientifically not necessary / other information available] ; the study does not need to be conducted because surface activity is not a desired property of the material [study scientifically not necessary / other information available]

Information requirement: Flash point

Reason: study technically not feasible

Justification: the study does not need to be conducted because the flash point is only relevant to liquids and low melting point solids [study technically not feasible]

Information requirement: Flammability

Reason: other justification

Justification: see 'Remark' - The test item can be predicted to not be classified as a readily combustible solid under Division 4.1, in compliance with Regulation (EC) No 1272/2008 of 16 December 2008, on Classification, Labelling and Packaging of Substances and Mixtures, and therefore no testing was performed as detailed in Method N.1 of the United Nations Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria, fifth revised edition 2009. the test item already represents the only commonly occurring oxide of palladium and therefore no further combustion products can be generated

Information requirement: Explosive properties

Reason: study scientifically not necessary / other information available

Justification: the study does not need to be conducted because there are no chemical groups present in the molecule which are associated with explosive properties [study scientifically not necessary / other information available]

Discussion of physicochemical properties

Additional information:

Physico-chemical endpoints for this substance are filled using test data generated as part of the REACH registration process and appropriate data waivers.



2. MANUFACTURE AND USES

2.1. Manufacture

Table 2.1. Manufacture

	Manufacture
M-1	<p>Manufacture of the substance (as such) <u>Further description of manufacturing process:</u></p> <p>Palladium dihydroxide mixtures are prepared by rising the pH of a formulation containing water soluble Palladium (II) salts solution in the presence of various metal oxide materials.</p> <p>Contributing activity/technique for the environment : - Manufacture of the substance (as such and in mixture) (ERC1)</p> <p>Contributing activity/technique for the workers : - Batch reaction in closed system (PROC 3) - Handling of solutions/Wet chemistry in open or semi-closed processes (PROC 4) - Mixing, blending (PROC 5) - Handling/Transfer of solutions (PROC 8b) - Small scale handling/Transfer of solutions (PROC 9) - Laboratory analyses (PROC 15) - Mechanical operations in open or semi-closed processes (PROC 24) - Wet cleaning (PROC 8a)</p> <p>use registered according to REACH Article 10; total tonnage manufactured/imported >=10tonnes/year per registrant Tonnage of substance for that use: <=100 tonnes/year Related assessment: use assessed in a joint CSR</p>

2.2. Identified uses

Table 2.2. Uses at industrial sites

	Uses at industrial sites
IW-1	<p>Use as an intermediate <u>Further description of the use:</u></p> <p>Contributing activity/technique for the environment : - Use as an intermediate (ERC6a)</p> <p>Contributing activity/technique for the workers : - Handling/Transfer of solutions (PROC 8b) - Small scale handling/transfer of solutions (PROC 9) - Batch reaction process in closed system (PROC 3) - Open or semi-closed wet chemical reaction process (PROC 4) - Mixing, blending (PROC 5) - Laboratory analyses (PROC 15) - Manual handling of wetted materials (PROC 26) - Process steps at elevated temperature (PROC 22) - Wet cleaning (PROC 8a)</p> <p>Sector of end use: SU 9: Manufacture of fine chemicals Technical function of the substance: intermediate (precursor)</p> <p>use registered according to REACH Article 10; total tonnage manufactured/imported >=10tonnes/year per registrant Tonnage of substance for that use: <=100 tonnes/year Substance supplied to that use: as such ; in a mixture Subsequent service life relevant for that use: no</p>



	Related assessment: use assessed in a joint CSR
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3. CLASSIFICATION AND LABELLING

3.1. Classification and labelling according to CLP / GHS

Substance: [Palladium dihydroxide](#)

Implementation: EU

Related composition: [Boundary composition](#)

Table 3.1. Classification and labelling according to CLP / GHS for physicochemical properties

Hazard class	Hazard category	Hazard statement	Reason for no classification
Explosives:			data conclusive but not sufficient for classification
Desensitised explosives:			data lacking
Flammable gases and chemically unstable gases:			data conclusive but not sufficient for classification
Aerosols:			data conclusive but not sufficient for classification
Chemicals under Pressure:			hazard class not assessed
Oxidising gases:			data conclusive but not sufficient for classification
Gases under pressure:			data conclusive but not sufficient for classification
Flammable liquids:			data conclusive but not sufficient for classification
Flammable solids:			data conclusive but not sufficient for classification
Self-reactive substances and mixtures:			data conclusive but not sufficient for classification
Pyrophoric liquids:			data conclusive but not sufficient for classification
Pyrophoric solids:			data conclusive but not sufficient for classification
Self-heating substances and mixtures:			data conclusive but not sufficient for classification
Substances and mixtures which in contact with water emit flammable gases:			data conclusive but not sufficient for classification
Oxidising liquids:			data conclusive but not sufficient for classification
Oxidising solids:	Oxid. Solid 3	H272: May intensify fire; oxidiser.	



Organic peroxides:			data conclusive but not sufficient for classification
Corrosive to metals:			data conclusive but not sufficient for classification

Table 3.2. Classification and labelling according to CLP / GHS for health hazards

Hazard class	Hazard category	Hazard statement	Reason for no classification
Acute toxicity - oral:			data conclusive but not sufficient for classification
Acute toxicity - dermal:			data conclusive but not sufficient for classification
Acute toxicity - inhalation:			data conclusive but not sufficient for classification
Skin corrosion / irritation:			data conclusive but not sufficient for classification
Serious damage / eye irritation:	Eye Irrit. 2	H319: Causes serious eye irritation.	
Respiratory sensitisation:			data lacking
Skin sensitisation:			data conclusive but not sufficient for classification
Aspiration hazard:			data lacking
Reproductive Toxicity:			data conclusive but not sufficient for classification
Reproductive Toxicity: Effects on or via lactation:			data conclusive but not sufficient for classification
Germ cell mutagenicity:			data conclusive but not sufficient for classification
Carcinogenicity:			data lacking
Specific target organ toxicity – single exposure:			data conclusive but not sufficient for classification
Specific target organ toxicity – repeated exposure:			data conclusive but not sufficient for classification

Table 3.3. Classification and labelling according to CLP / GHS for environmental hazards

Hazard class	Hazard category	Hazard statement	Reason for no classification
Hazards to the aquatic environment (acute/short-term):			data conclusive but not sufficient for classification
Hazards to the aquatic environment (chronic/long-term):			data conclusive but not sufficient for classification
M-Factor acute:			
M-Factor chronic:			



Hazardous to the ozone layer:			data conclusive but not sufficient for classification
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Labelling

Signal word: Warning

Hazard pictogram:

GHS07: exclamation mark



GHS03: flame over circle

Hazard statements:

H272: May intensify fire; oxidiser.

H319: Causes serious eye irritation.

Precautionary statements:

P210: Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.

P220: Keep away from clothing or other combustible materials.

P264: Wash ... thoroughly after handling.

P280: Wear protective gloves/protective clothing/eye protection/face protection/hearing protection/...

P305+P351+P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

P370+P378: In case of fire: Use... to extinguish.

P337+P313: If eye irritation persists: Get medical advice/attention.

P501: Dispose of contents/container to ...



4. ENVIRONMENTAL FATE PROPERTIES

General discussion of environmental fate and pathways:

Key Information:

The log Kd for suspended particulate matter (SPM) in freshwater is 3.39 (stdev 0.40) and the average Kd is 2455 L/kg. Where wastewater is discharged to marine water it is recommended to use the measured partition coefficient in seawater, log Kd 4.21 (i.e. Kd is 16220 L/kg). The log Kd for soil is 2.64 (stdev 0.48) and the average Kd is 436.5 L/kg.

Additional information:

Information on the partitioning of palladium in the environment is taken from three published papers (Cobelo-Garcia et al. 2008, Sako et al. 2009, Turner et al. 2006) and Kd values have been calculated for suspended particulate matter in freshwater, seawater and soil.

Biodegradation and hydrolysis are not considered to be relevant endpoints for this substance.

4.1. Degradation

4.1.1. Abiotic degradation

4.1.1.1. Hydrolysis

No relevant information available.

Data waiving

Information requirement: Hydrolysis

Reason: study scientifically not necessary / other information available

Justification: see 'Remark' - In accordance with REACH Annex XI Section 1 testing does not appear to be scientifically necessary because this method is used on organic substances to measure the decomposition or degradation of a chemical reacting with water. For inorganics this type of method is not appropriate.

4.1.1.2. Phototransformation/photolysis

4.1.1.2.1. Phototransformation in air

No relevant information available.

4.1.1.2.2. Phototransformation in water

No relevant information available.

4.1.1.2.3. Phototransformation in soil

No relevant information available.

4.1.2. Biodegradation

4.1.2.1. Biodegradation in water

4.1.2.1.1. Screening tests

No relevant information available.

Data waiving

Information requirement: Biodegradation in water: screening test



Reason: study technically not feasible

Justification: the study does not need to be conducted because the substance is inorganic [study technically not feasible]

4.1.2.1.2. Simulation tests (water and sediments)

No relevant information available.

4.1.2.1.3. Summary and discussion of biodegradation in water and sediment

No relevant information available.

4.1.2.2. Biodegradation in soil

No relevant information available.

4.1.3. Summary and discussion of degradation

No information available.

4.2. Environmental distribution

4.2.1. Adsorption/desorption

The studies on adsorption/desorption are summarised in the following table:

Table 4.1. Studies on adsorption/desorption

Method	Results	Remarks
adsorption / desorption: screening batch equilibrium method Laboratory study, no guideline followed	Adsorption coefficient: log Kd: 3.59 at 23°C (Mean for all salinities, standard deviation 0.41) log Kd: 3.39 at 23°C (Mean for freshwaters, standard deviation 0.40) log Kd: 3.84 at 23°C (Mean for estuarine waters, standard deviation 0.04) log Kd: 4.21 at 23°C (Single value for seawater, salinity 33 %) Partition coefficients: Mass balance (in %) at end of adsorption phase: Mass balance (in %) at end of desorption phase: Transformation products:	2 (reliable with restrictions) key study experimental study Test material Palladium (II), Form: gas under pressure: refrigerated liquefied gas (full information in Annex II). Reference Cobelo-Garcia A, Turner A, Millward G. 2008
adsorption / desorption: screening batch equilibrium method Laboratory study, no guideline followed	Adsorption coefficient: log Kd: 2.64 at 25°C (Overall mean, standard deviation 0.48) Partition coefficients: Mass balance (in %) at end of adsorption phase: Mass balance (in %) at end of desorption phase:	2 (reliable with restrictions) supporting study experimental study Test material Palladium (II), Form: gas under pressure: refrigerated



	Transformation products:	liquefied gas (full information in Annex II). Reference Sako A, Lopes L, Roychoudhury A 2009
adsorption / desorption: screening batch equilibrium method Laboratory study, no guideline followed	Adsorption coefficient: log Kd: >2.7 - <3 at 20°C (Dependent on treatment of the sediment material) Partition coefficients: Mass balance (in %) at end of adsorption phase: Mass balance (in %) at end of desorption phase: Transformation products:	2 (reliable with restrictions) supporting study experimental study Test material Palladium (II), Form: gas under pressure: refrigerated liquefied gas (full information in Annex II). Reference Turner A, Crussell M, Millward G, Cobelo-Garcia A, Fisher A 2006

Discussion

The following information is taken into account for any environmental exposure assessment:

Key Information:

The log Kd for suspended particulate matter (SPM) in freshwater is 3.39 (stdev 0.40) and the average Kd is 2455 L/kg. Where wastewater is discharged to marine water it is recommended to use the measured partition coefficient in seawater, log Kd 4.21 (i.e. Kd is 16220 L/kg). The log Kd for soil is 2.64 (stdev 0.48) and the average Kd is 436.5 L/kg.

Value used for CSA:

Koc at 20°C:

Other adsorption coefficients:

log Kp (solids-water in soil) : 2.64 at 25°C

log Kp (solids-water in suspended matter) : 3.39 at 23°C

Relevant studies: Adsorption / desorption. Supporting study - Sako 2009

Relevant studies: Adsorption / desorption. Supporting study - Turner 2006

Relevant studies: Adsorption / desorption. Key study - Cobelo-Garcia 2008

Additional information:

Two high quality studies have determined the partitioning of Pd between river water and suspended particulate matter. Both studies showed relatively consistent results for experiments performed in freshwaters, and similar partitioning was also observed in both estuarine and marine water in the key study (Turner et al., 2006; Cobelo-Garcia et al., 2008). A high quality study of the partitioning of palladium to two soils and one sediment provides information relevant to the soil compartment (Sako et al., 2009).



Average partition coefficients have been derived in cases where multiple partition coefficients are available for the same type of system (e. g. partitioning to suspended particulate matter in surface waters). The average values have been derived by calculating the log values of the individual partition coefficients (Kd). Following log transformation, the mean and standard deviation are calculated to define an “average” partition coefficient and its associated standard deviation, assuming a log-normal distribution of Kd values. The log Kd across all waters studied is 3.59 and the average Kd across all salinities is 3890.5 L/kg (st dev 0.41). Averaging of Kd values obtained from tests at different salinities hides a clear difference in the partitioning behaviour of palladium between fresh and marine waters, with stronger partitioning being observed in marine water. Consequently, separate Kd values are recommended for assessments of freshwater and marine systems. The log Kd for freshwater is 3.39 (stdev 0.40) and the average Kd is 2455 L/kg. The log Kd for marine water is 4.21, and the Kd is 16220 L/kg. The log Kd for soil is 2.64 (stdev 0.48) and the average Kd is 436.5 L/kg.

4.2.2. Volatilisation

No relevant information available.

4.2.3. Distribution modelling

No relevant information available.

4.2.4. Summary and discussion of environmental distribution

4.3. Bioaccumulation

4.3.1. Aquatic bioaccumulation

No relevant information available.

4.3.2. Terrestrial bioaccumulation

No relevant information available.

4.3.3. Summary and discussion of bioaccumulation

4.4. Secondary poisoning

Based on the available information, there is no indication of a bioaccumulation potential and, hence, secondary poisoning is not considered relevant (see CSR chapter 7.5 “PNEC derivation and other hazard conclusions”).



5. HUMAN HEALTH HAZARD ASSESSMENT

5.1. Toxicokinetics (absorption, metabolism, distribution and elimination)

5.1.1. Non-human information

No relevant information available.

5.1.2. Human information

No relevant information available.

5.1.3. Summary and discussion of toxicokinetics

The following information is taken into account for any hazard / risk assessment:

Key Information:

Despite a low water solubility (<0.1 mg/L), a high oral availability is anticipated based on significant bio-elution in simulated gastric fluid (cf Rodriguez 2012a,b in section 7.12) and a relatively low molecular weight (~140 g/mol). It is therefore likely that palladium dihydroxide will be absorbed (as the ions) from the gastro intestinal tract. As such, predicted oral absorption of palladium dihydroxide is conservatively set at 100%.

Although not expected to reach the lungs in appreciable quantities (based on respiratory tract deposition modelling data - cfr Selck and Parr 2011 in IUCLID section 4.5), as a relatively low molecular weight compound, any palladium dihydroxide reaching the lungs has the potential to be absorbed through aqueous pores. As such, the predicted inhalation absorption is conservatively set at 100%. Palladium dihydroxide, with water solubility of <0.1 mg/L (cfr. Skaeff 2012 a,b and O'Connor 2011 in IUCLID Section 4.8), may not exhibit appreciable uptake by the dermal route (HERAG Guidance 'Assessment of occupational dermal exposure and dermal absorption for metals and inorganic metal compounds' at <https://www.icmm.com/en-gb/guidance/mining-metals/herag>), especially considering the low dermal penetration expected from metall. Moreover, palladium dihydroxide is demonstrated to lack skin irritation potential (which could, in theory, disrupt skin barrier function). As such, predicted dermal absorption is set at 10%.

Once absorbed, distribution and excretion are expected to be rapid, with little or no bioaccumulation occurring. The potential for bioaccumulation of certain other metals and ions is recognised.

Value used for CSA:

Bioaccumulation potential: low bioaccumulation potential

Absorption rate - oral (%): 100

Absorption rate - dermal (%): 10

Absorption rate - inhalation (%): 100

Additional information:

Absorption

Good-quality information on absorption of palladium compounds is very limited. In general, a compound needs to be dissolved before it can be taken up from the gastro-intestinal tract after oral administration. Experts from the IPCS reported that absorption of palladium ions from the gastrointestinal tract is poor, a view based on a study where adult and suckling rats absorbed less than 0.5% and about 5%, respectively, of a single oral dose of radiolabelled (¹⁰³Pd) palladium dichloride (IPCS, 2002). Experts from the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) used an oral absorption figure of 10% when converting an oral permitted daily exposure figure for palladium compounds to a parenteral equivalent (ICH, 2014). While palladium dihydroxide is estimated to be essentially



insoluble in water (<0.1 mg/L; Skeaff, 2012), a bio-elution test with the compound showed that the proportion of metal release (from total metal content) in simulated gastric fluid was 77.8% after 2 hours, indicating a high oral availability of the compound. Moreover, based on expert ECHA guidance, as the molecular weight is low (~140 g/mol i.e. less than 200 g/mol), the substance may pass through aqueous pores or be carried through the epithelial barrier by the bulk passage of water. A health-precautionary assumption is that the ions will be absorbed from the gastro-intestinal tract. As such, predicted oral absorption of palladium dihydroxide is set at 100%.

In an acute oral study on the structurally related compound palladium dichloride, necropsy of deceased animals revealed changes in the lungs, liver, kidneys, stomach and small intestine (Allen, 1994a), at least some of which indicate a degree of absorption. In a combined repeated dose and reproductive/developmental toxicity dietary study, palladium dihydroxide induced increases in liver weight in females and decreases in seminal vesicle weight in males (Török-Bathó, 2015), again indicating a degree of oral absorption. [Macroscopic and microscopic effects in the stomach, ileum, caecum, colon and rectum were also seen but could reflect local toxicity.]

No good-quality data were found regarding absorption of palladium compounds following inhalation. One Expert Group noted that, following a single intratracheal or inhalation (7.2 mg/m³; aerodynamic diameter around 1 µm) exposure to 103Pd-radiolabeled palladium dichloride in rats, absorption/retention was higher than was observed for oral administration (i.e. >5%) but did not differentiate between absorption and mere retention in the respiratory tract (IPCS, 2002). Vapour pressure testing was waived on the basis of palladium dihydroxide having a high melting point (decomposition at 60°C with no definitive signs of melting below 450°C; Walker, 2011b). Particle size distribution (PSD) data, as measured by simple sieving, indicate that only a small proportion (13.1%) of the compound is <100 µm (Walker, 2011c). However, in another PSD study, on the substance as a liquid dispersion, the 10th, 50th and 90th percentile average particle sizes for palladium dihydroxide were 0.27, 0.67 and 12.1 µm, respectively (Potthoff, 2012). Moreover, dustiness testing, a more energetic PSD measurement, with the compound returned a mass median aerodynamic diameter (MMAD) value of 29.8 µm (Parr, 2011; Selck and Parr, 2011). In contradiction with the granulometry data, an MMAD value <100 µm indicates that a significant proportion of the substance is likely to be inhalable. Nevertheless, respiratory tract deposition modelling with the dustiness data yielded output values of 46.6, 0.16 and 0.19% for the nasopharyngeal (head), tracheobronchial (TB) and pulmonary regions of the respiratory tract, respectively. This indicates that very little airborne substance (<1%) will be deposited in the lower regions of the human respiratory tract, i.e. the TB or pulmonary regions via oronasal normal augmented breathing.

Most of the inhaled fraction is likely to be retained in the head region and, based on a low water solubility (<0.1 mg/L) could be coughed or sneezed out of the body or swallowed, with systemic uptake being determined predominantly by oral bioavailability. The insoluble nature of the compound would limit any diffusion/dissolution into the mucus lining the respiratory tract. However, any palladium dihydroxide which is able to migrate into the mucus has the potential to be absorbed directly across the respiratory tract epithelium by passive diffusion. Less than 1% of the inhaled fraction is likely capable of reaching the alveoli. Thus, absorption via the lungs will not be a significant type of exposure. Any palladium dihydroxide reaching the lungs would mainly be engulfed by alveolar macrophages and translocated out of the respiratory tract. Overall, while it is very unlikely that palladium dihydroxide will be available to a high extent via inhalation, it is considered health precautionary in the light of the lack of specific absorption data, to take forward the ECHA default inhalation absorption value of 100%.

No good-quality data were found regarding absorption following dermal exposure to palladium compounds. One Expert Group noted that “palladium was found in all internal organs examined” after dermal treatment of rabbits with “palladium hydrochloride” (formula not specified) or guinea pigs with chloropalladosamine, but quantitative absorption data were not given (IPCS, 2002). Estimation of dermal absorption is based on relevant available information (mainly water solubility, molecular weight and log Pow) and expert judgement. Partition coefficient testing was waived on the basis of the inorganic nature of substance. Given the insoluble nature of palladium dihydroxide (<0.1 mg/L), dermal uptake is likely to be low. In spite of this, in the light of the limited available experimental data, ECHA guidance indicates that a default value of 100% dermal absorption should be used (ECHA, 2014). Nevertheless, specific guidance on the health risk assessment of metals indicates that molecular weight and log Pow considerations do not apply to these substances (“as inorganic compounds require dissolution involving dissociation to metal cations prior to being able to penetrate skin by diffusive mechanisms”) and tentatively proposes dermal absorption figures: 1.0 and 0.1% following exposure to liquid/wet media and dry (dust) respectively (ICMM, 2007). Further, palladium dihydroxide is not classified for skin irritation. This is based on the lack of irritation potential observed both in vitro and in vivo with the



structurally related compounds palladium dichloride and palladium monoxide (Allen, 1994b; Campbell et al., 1975). Moreover, in a bio-elution test with palladium dihydroxide, the proportion of metal release (from total metal content) in simulated dermal fluid was 1.045 and 2.60% after 24 and 168 hours respectively, indicating a low dermal availability of the compound. Given the low penetration expected from metals, and the low water solubility (and, thus, low expected dermal bioavailability), it is suitably health precautionary to take forward the lower of the two ECHA default values for dermal absorption, of 10%, for the safety assessment of palladium dihydroxide.

No clinical signs of toxicity were seen in *in vivo* skin irritation (Allen, 1994b; Campbell et al., 1975) and skin sensitisation (Wahlberg and Boman, 1990, 1992; Schuppe et al., 1998) studies on the “uncomplexed and partially-complexed palladium compounds” category members palladium monoxide and palladium dichloride. While these studies would have been limited in their assessment of systemic effects, the data overall suggest that the substance will not be well-absorbed dermally.

Distribution/Metabolism

Once absorbed, distribution of palladium and hydroxide ions throughout the body is expected based on water solubility of the ions and a relatively low substance molecular weight.

Necropsy changes in the lungs, liver and kidneys (as well as stomach and small intestine) in an acute oral study on the structurally related compound palladium dichloride (Allen, 1994a) indicate possible distribution to these organs. In a combined repeated dose and reproductive/developmental toxicity dietary study, palladium dihydroxide induced increases in liver weight in females and decreases in seminal vesicle weight in males (Török-Bathó, 2015), suggesting possible distribution to these organs.

When rats were given potassium hexachloropalladate in the drinking water at 0, 10, 100 or 250 mg/L for 90 days, absorbed Pd was found mainly in the kidneys and it did not accumulate in liver, lung, spleen or bone tissue (Iavicoli et al., 2010). IPCS noted that, after single oral, intravenous or intratracheal doses of palladium salts or complexes to rats, rabbits or dogs, the highest palladium concentrations were found in kidney, liver, spleen, lymph nodes, adrenal gland, lung and bone (IPCS, 2002).

Elimination

In rats given potassium hexachloropalladate in the drinking water at up to 250 mg/L for 90 days, elimination was rapid and primarily through the faecal route, although small amounts were found in the urine at the highest dose level (Iavicoli et al., 2010).

Despite displaying poor water solubility, bio-elution test data indicate that a significant proportion of the metal is released in simulated gastric fluid. As such, rapid excretion is likely based on a high water solubility and low substance molecular weight. It is noted that certain metals and ions may interact with the matrix of the bone, causing them to accumulate within the body (ECHA, 2014). However, as an ionic substance, palladium dihydroxide is considered to have only a low potential for bioaccumulation based on a low anticipated affinity for the lipophilic tissues.

Conclusion

Based on the physico-chemical properties, the chemical structure, molecular weight and the results of toxicity and bio-elution studies, as well as limited toxicokinetic data on other palladium compounds, palladium dihydroxide is likely partially bioavailable by the oral route and rapidly excreted once absorbed. A high dermal bioavailability is unlikely, particularly as the substance is an inorganic powder with a lack of skin irritation potential and unfavourable bio-elution parameters. Although bioavailability by the inhalation route is anticipated to be low (based on respiratory tract deposition modelling data), inhalation absorption is considered a possibility based on its low molecular weight. Proposed predicted absorption figures for the oral, dermal and inhalation routes are 100, 10 and 100%, respectively.

5.2. Acute toxicity

5.2.1. Non-human information

5.2.1.1. Acute toxicity: oral



The results of studies on acute toxicity after oral administration are summarised in the following table:

Table 5.1. Studies on acute toxicity after oral administration

Method	Results	Remarks
<p>rat [common species] (Sprague-Dawley [rat]) male oral: gavage no guideline followed In the lethal dose experiments, male Sprague-Dawley rats received the tested palladium salt by gavage and were observed through a 14-day period. The LD50 values were calculated by the method of Litchfield and Wilcoxon. The exact dosing strategy is unclear and no details on pathological assessment are given.</p>	<p>LD50: >4900 mg/kg bw (male) based on: (test mat.) (CL was not determined)</p>	<p>2 (reliable with restrictions) key study experimental study</p> <p>Test material palladium monoxide / 1314-08-5 / 215-218-3, Form: not specified (full information in Annex II).</p> <p>Reference Holbrook DJ, Washington ME, Leake HB and Brubaker PE 1975</p>
<p>rat [common species] (Sprague-Dawley [rat]) male oral: gavage no guideline followed In the lethal dose experiments, male Sprague-Dawley rats received the tested palladium salt by gavage and were observed through a 14-day period. The LD50 values were calculated by the method of Litchfield and Wilcoxon. The exact dosing strategy is unclear and no details on pathological assessment are given.</p>	<p>LD50: >4900 mg/kg bw (male) based on: (test mat.) (CL was not determined)</p>	<p>2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate)</p> <p>Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, (full information in Annex II).</p> <p>Reference Holbrook DJ, Washington ME, Leake HB and Brubaker PE 1975</p>
<p>Justification for type of information: Substance considered to fall within the scope of the read-across category 'Palladium, Palladium monoxide and Palladium dihydroxide'</p>		
<p>Weight-of-Evidence argumentation</p>	<p>LD50: >2000 mg/kg bw based on: (test mat.)</p>	<p>2 (reliable with restrictions) weight of evidence weight of evidence justification</p> <p>Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, (full information in</p>



		Annex II). Reference European Precious Metals Federation 2021
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5.2.1.2. Acute toxicity: inhalation

No relevant information available.

Data waiving

Information requirement: Acute toxicity after inhalation exposure

Reason: other justification

Justification: the study does not need to be conducted because exposure of humans via inhalation is not likely taking into account the vapour pressure of the substance and/or the possibility of exposure to aerosols, particles or droplets of an inhalable size [exposure considerations] ; see 'Remark' - In accordance with Column 2 of REACH Annex VIII, this study does not need to be conducted as human exposure via inhalation of aerosols, particles or droplets of an inhalable size is unlikely. Particle size distribution (PSD) data, as measured by simple sieving, indicates that only a small proportion (13.1%) of palladium dihydroxide is <100 µm (Walker, 2011c). However, in another PSD study, on the substance as a liquid dispersion, the 10th, 50th and 90th percentile average particle sizes for palladium dihydroxide were 0.27, 0.67 and 12.1 µm, respectively (Potthoff, 2012). Moreover, dustiness testing, a more energetic PSD measurement, with the compound returned a mass median aerodynamic diameter (MMAD) value of 29.8 µm (Parr, 2011; Selck and Parr, 2011). An MMAD value <100 µm indicates that a significant proportion of a substance is likely to be inhalable. Respiratory tract deposition modelling with the dustiness data yielded output values of 46.6, 0.16 and 0.19% for the nasopharyngeal (head), tracheobronchial (TB) and pulmonary regions of the respiratory tract, respectively. Hence, very little airborne substance (<1%) is expected to deposit in the lower regions of the human respiratory tract, i.e. the TB or pulmonary regions via oronasal normal augmented breathing. Most of the inhaled fraction is likely to be retained in the head region and could be coughed or sneezed out of the body or swallowed, with systemic uptake being determined predominantly by oral bioavailability. Thus, inhalation will not be a significant route of exposure. Therefore, for animal welfare reasons, conducting new in vivo toxicity tests is considered a last resort. No testing by the inhalation route is considered justified.

5.2.1.3. Acute toxicity: dermal

No relevant information available.

Data waiving

Information requirement: Acute toxicity after dermal administration

Reason: study scientifically not necessary / other information available

Justification: the study does not need to be conducted because the physicochemical and toxicological properties suggest no potential for a significant rate of absorption through the skin [study scientifically not necessary / other information available] ; See 'Remark' - No studies involving dermal (or acute oral) application of palladium hydroxide are available. However, there is a study on palladium monoxide who is a member of the read-across category 'Palladium, Palladium monoxide and Palladium dihydroxide'. The existing in vivo skin irritation study on palladium monoxide (Campbell et al., 1975), albeit limited in its assessment of systemic toxicity, indicates a lack of acute systemic toxicity following dermal exposure. Exposure considerations provide good support for the conclusion that an acute dermal toxicity study can be waived. First, palladium dihydroxide is a solid (Walker and White, 2011) and skin contact during production and/or use is expected to be very low. Second, palladium dihydroxide is classified for eye irritation, so appropriate safety labelling, personal protection and RMMs/OCs are required. These will ensure that the potential for skin exposure is minimised. As such, there are sufficient available data for chemical hazard and risk assessment, classification and labelling, and risk mitigation purposes. Further, specific guidance on the health risk assessment of metals (ICMM, 2007) indicates low dermal absorption (up to 1.0%). In bio-elution



tests with palladium dihydroxide, the proportion of metal release (from total metal content) in simulated dermal fluid was similarly low: 1.045 and 2.60% after 24 and 168 hours, respectively (Rodriguez, 2012 – cf. IUCLID section 7.12). Finally, for animal welfare reasons, conducting new in vivo toxicity tests is considered as a last resort. As such, no further testing is considered justified.

5.2.1.4. Acute toxicity: other routes

No relevant information available.

5.2.2. Human information

No relevant information available.

5.2.3. Summary and discussion of acute toxicity

The following information is taken into account for any hazard / risk assessment:

Key Information:

No relevant acute oral, dermal or inhalation toxicity data were identified with palladium dihydroxide. Via a weight-of-evidence argumentation, the registrants consider it justified to avoid in vivo testing for acute toxicity(oral) for this substance (as exemplified in ECHA Guidance R.7a Figure 7.4-4) and consider the substance of low acute hazard via the oral route with an assumed LD50>2000 mg/kg(bw). Based on this experimental evidence, palladium dihydroxide is considered to have an LD50>2000 mg/kg(bw).

The substance is also considered to fall within the scope of the read-across category 'Palladium, palladium monoxide and Palladium dihydroxide'. In an acute oral toxicity study, groups of male Sprague-Dawley rats were administered palladium monoxide by stomach tube and observed for 14 days. Using the prescribed statistical method, the acute oral median lethal dose (LD50) was found to exceed 4.9 g/kg bw.

Value used for CSA:

Acute oral toxicity:

no adverse effect observed
(LD50) >2000 mg/kg bw

Acute dermal toxicity:

no study available

Acute inhalation toxicity:

no study available

Relevant studies: Acute toxicity: oral.WoE(EPMF, 2021)

Relevant studies: Acute toxicity: oral (KEY)_PdO_Holbrook et al. (1975).source

Relevant studies: Acute toxicity: oral (KEY)_PdO_Holbrook et al. (1975).target

Additional information:

No relevant human or laboratory animal acute toxicity data were identified with palladium dihydroxide as test item.

Via a weight-of-evidence argumentation, the registrants consider it justified to avoid in vivo testing for acute toxicity(oral) for this substance (as exemplified in ECHA Guidance R.7a Figure 7.4-4) and consider the substance of low acute hazard via the oral route with an assumed LD50>2000 mg/kg(bw).

The substance is considered to fall within the scope of the read-across category 'Palladium, palladium monoxide and Palladium dihydroxide'. In an acute oral toxicity study, groups of male Sprague-Dawley rats were administered palladium monoxide by stomach tube and observed for 14 days. Using the prescribed statistical method, the acute oral median lethal dose (LD50) was found to exceed 4.9 g/kg bw.

Based on this experimental evidence, palladium dihydroxide is considered to have an LD50>2000 mg/kg(bw).



The substance is not expected to reach the lungs in appreciable quantities (based on respiratory tract deposition modelling data). Thus, inhalation will not be a significant route of exposure (Selck and Parr 2012 a,b - cf section 4.5).

Since a substance is required to be bioavailable in order to induce systemic toxicity following acute exposure, palladium dihydroxide is not considered to pose an acute toxicity hazard. Finally, for animal welfare reasons, conducting new in vivo toxicity tests is considered a last resort. Consequently, no testing for acute toxicity of palladium dihydroxide is considered justified.

Justification for classification or non classification:

No acute toxicity data are available for palladium dihydroxide. However, such effects are not expected, based on a lack of bioavailability following exposure via the oral, dermal and inhalation routes, and read-across from palladium monoxide and palladium dihydroxide. As such, there is no evidence to classify palladium dihydroxide for acute toxicity according to EU CLP criteria (EC 1272/2008).

5.3. Irritation

5.3.1. Skin

5.3.1.1. Non-human information

The results of studies on skin irritation are summarised in the following table:

Table 5.2. Studies on skin irritation

Method	Results	Remarks
rabbit [common species] (albino) Coverage: occlusive (Pairs of test sites, each 2 cm x 2 cm, on the closely clipped dorsolaterals aspects of each animal, one side abraded and the other side intact) Vehicle: water - 0.1 ml no guideline followed Dermal irritancy assessed using male albino rabbits using procedures and evaluation criteria adopted from those in use by the National Institute for Occupational Safety and Health, ... a modification of the official Food and Drug Administration procedure [1973]"	GHS criteria not met overall irritation score 0 of max. 4 (Time point: 24 and 72 hours) (Severity rating for both intact and abraded skin sites)	2 (reliable with restrictions) key study experimental study Test material palladium monoxide / 1314-08-5 / 215-218-3, (full information in Annex II). Reference Campbell KI, George EL, Hall LL and Stara JF 1975
rabbit [common species] (albino) Coverage: occlusive (Pairs of test sites, each 2 cm x 2 cm, on the closely clipped dorsolaterals aspects of each animal, one side abraded and the other side intact) Vehicle: water - 0.1 ml no guideline followed Dermal irritancy assessed using male albino rabbits using procedures and evaluation criteria adopted from those in use by the National Institute for Occupational Safety and Health, ... a modification of the official Food and Drug Administration procedure [1973]"	not irritating - Migrated information Criteria used for interpretation of results: other: evaluation criteria adopted from those in use by the National Institute for Occupational Safety and Health overall irritation score 0 of max. 4 (Time point: 24 and 72 hours) (Severity rating for both intact and abraded skin sites)	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, (full information in Annex II).



		Reference Campbell KI, George EL, Hall LL and Stara JF 1975
Justification for type of information: Substance considered to fall within the scope of the read-across category 'Palladium, Palladium monoxide and Palladium dihydroxide'		
Coverage: Vehicle: according to guideline MatTek Corporation Protocol: In vitro EpiDerm™ Skin Irritation Test (EPI-200-SIT) For use with MatTek Corporation's Reconstructed Human Epidermal Model EpiDerm (EPI-200-SIT); Version 10 February 2019 ; according to guideline EU Method B.46 (In Vitro Skin Irritation: Reconstructed Human Epidermis Model Test) ; according to guideline OECD Guideline 439 (In Vitro Skin Irritation: Reconstructed Human Epidermis Test Method)	GHS criteria not met % tissue viability Value: 78.94 (no indication of irritation)	1 (reliable without restriction) key study experimental study Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, (full information in Annex II). Reference Spohr 2021

Studies with results indicating corrosivity to the skin are summarised in section 5.4 Corrosivity.

5.3.1.2. Human information

No relevant information available.

5.3.2. Eye

5.3.2.1. Non-human information

The results of studies on eye irritation are summarised in the following table:

Table 5.3. Studies on eye irritation

Method	Results	Remarks
rabbit (not specified) Vehicle: not specified according to guideline CFR 21, part 191.12 (revised as of April 1, 1973)	Category 1 (irreversible effects on the eye) - Migrated information Criteria used for interpretation of results: EU Number of animals showing irritant reactions (Total number of test animals) 6 of max. 6 (Time point: 24 hours) not reversible Number of animals showing irritant reactions (Total number of test animals) 6 of max. 6 (Time point: 48 hours) not reversible Number of animals showing irritant reactions	2 (reliable with restrictions) key study experimental study Test material palladium(2+) dichloride / 7647-10-1 / 231-596-2, Form: not specified (full information in Annex II). Reference Hysell D, Neiheisel S and Cmeheil D 1974 IPCS 2002



	(Total number of test animals) 6 of max. 6 (Time point: 72 hours) not reversible	Stara JF 1974
rabbit (not specified) Vehicle: not specified according to guideline CFR 21, part 191 12 (revised as of April 1, 1973)	not irritating - Migrated information Criteria used for interpretation of results: EU Number of animals showing irritant reactions (Total number of test animals) 0 of max. 6 (Time point: 24 hours) Not applicable Number of animals showing irritant reactions (Total number of test animals) 0 of max. 6 (Time point: 48 hours) Not applicable Number of animals showing irritant reactions (Total number of test animals) 0 of max. 6 (Time point: 72 hours) Not applicable	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) Test material palladium(2+) dihydroxide / 12135- 22-7 / 235-219-2, Form: solid: particulate/powder - migrated information: powder (full information in Annex II). Reference Hysell D, Neiheisel S and Cmehil D 1974 IPCS 2002 Stara JF 1974
Justification for type of information: Substance considered to fall within the scope of the read-across category 'Palladium, Palladium monoxide and Palladium dihydroxide'		
in vitro study cattle Vehicle: physiological saline - The test item was ground in a mortar with a pistil to improve its consistency and tested as a 20% suspension (w/v) in saline using sonication for 10 minutes. according to guideline EU method B.47 (Bovine corneal opacity and permeability test method for identifying ocular corrosives and severe irritants) ; according to guideline OECD Guideline 437 (Bovine Corneal Opacity and Permeability Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage) [from 26 July 2013]	No prediction can be made in vitro irritation score value 5.87	1 (reliable without restriction) key study experimental study Test material palladium(2+) dihydroxide / 12135- 22-7 / 235-219-2, (full information in Annex II). Reference Sokolowski 2021
in vitro study The EpiOcular tissue construct is a non- keratinized epithelium prepared from normal human keratinocytes. It models the cornea epithelium with progressively stratified, but not cornified cells. These	study cannot be used for classification - This value is below the threshold for irritancy of ≤ 60%. Therefore, no prediction can be made for Palladium dihydroxide from this result. mean percent tissue viability	1 (reliable without restriction) key study experimental study



cells are not transformed or transfected with genes to i Vehicle: unchanged (no vehicle) - The test item was tested neat. according to guideline MatTek Corporation Protocol: EpiOcular™ Eye Irritation Test (OCL-200-EIT) for the prediction of acute ocular irritation of chemicals; for use with MatTek Corporation's Reconstructed Human EpiOcular™ Model; MK-24-007-005 ; according to guideline OECD Guideline 492 (Reconstructed Human Cornea-like Epithelium (RhCE) Test Method for Identifying Chemicals Not Requiring Classification and Labelling for Eye Irritation or Serious Eye Damage)	value 34.24	Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, (full information in Annex II). Reference Spohr 2021
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5.3.2.2. Human information

No relevant information available.

5.3.3. Respiratory tract

5.3.3.1. Non-human information

No relevant information available

5.3.3.2. Human information

No relevant information available.

5.3.4. Summary and discussion of irritation

The following information is taken into account for any hazard / risk assessment:

Key Information:

In in vitro studies according to OECD431 and OECD439, Palladium dihydroxide was shown to be non corrosive and non-irritant to skin according to UN GHS and EU CLP regulation.

Palladium dihydroxide is considered to fall within the scope of the read-across category of 'Palladium, Palladium monoxide and Palladium dihydroxide'. Palladium monoxide was not irritant in a limited (pre-GLP) study, involving 24-hr occluded application to the intact and abraded skin of 6 male rabbits.

The eye irritation/corrosion potential of palladium dihydroxide was tested in two in vitro assays (OECD437 and OECD492). However, under the experimental conditions reported, a prediction for the eye damage hazard could not be made (GHS) for Palladium dihydroxide.

Palladium dihydroxide is considered to fall within the scope of the read-across category of 'Palladium, Palladium monoxide and Palladium dihydroxide'. According to an expert review of an unpublished eye irritation study, conducted to US guidelines (CFR 21, part 191.12), a single instillation of palladium monoxide (100 mg) to the eyes of six rabbits produced no signs of irritation.

The water solubility and dermal bioaccessibility of palladium dihydroxide was low (Skaeff 2012; O'Connor 2011). Although the dermal bio-elution testing does not extend to the use of simulation lachrymal fluid, the available simulation dermal fluid data is nevertheless indicative of negligible bioavailability following exposure



via the eyes. Since a chemical is required to be bioavailable in order to induce (non-mechanical) irritation, and since the substance has no pH <2 or >11, palladium dihydroxide is considered incapable of inducing eye corrosion. Therefore, and driven by the inconclusive in vitro data, the registrants consider it justified to not perform further in vivo mammalian testing but instead classify the substance as Eye Irritant cat 2 (H319).

Value used for CSA:

Skin irritation / corrosion: no adverse effect observed (not irritating) Eye irritation: adverse effect observed (irritating) Respiratory irritation: no study available

Relevant studies: Skin irritation / corrosion_PdO_Campbell et al. (1975).source

Relevant studies: Skin irritation / corrosion_Pd dihydroxide_OECD439_Spohr(2021)

Relevant studies: Skin irritation / corrosion_Pd dihydroxide_OECD431_Spohr(2021)

Relevant studies: Skin irritation / corrosion_PdO_Campbell et al. (1975).target

Relevant studies: Eye irritation_Pd dihydroxide_BCOP(OECD437)_Sokolowski(2021).004

Relevant studies: Eye irritation_EpiOcular_Spohr(2021).005

Relevant studies: Eye irritation (KEY)_PdO_Hysell et al. (1974).source

Relevant studies: Eye irritation, (KEY)_PdO_Hysell et al. (1974).target

Additional information:

In in vitro studies according to OECD431 and OECD439, Palladium dihydroxide was shown to be non corrosive and non-irritant to skin according to UN GHS and EU CLP regulation.

Palladium dihydroxide is considered to fall within the scope of the read-across category of 'Palladium, Palladium monoxide and Palladium dihydroxide'. Palladium monoxide was not irritant in a limited (pre-GLP) study, involving 24-hr occluded application to the intact and abraded skin of 6 male rabbits.

The eye irritation/corrosion potential of palladium dihydroxide was tested in two in vitro assays (OECD437 and OECD492). However, under the experimental conditions reported, a prediction for the eye damage hazard could not be made (GHS) for Palladium dihydroxide.

Palladium dihydroxide is considered to fall within the scope of the read-across category of 'Palladium, Palladium monoxide and Palladium dihydroxide'. According to an expert review of an unpublished eye irritation study, conducted to US guidelines (CFR 21, part 191.12), a single instillation of palladium monoxide (100 mg) to the eyes of six rabbits produced no signs of irritation.

The water solubility and dermal bioaccessibility of palladium dihydroxide was low (Skaeff 2012; O'Connor 2011). Although the dermal bio-elution testing does not extend to the use of simulation lachrymal fluid, the available simulation dermal fluid data is nevertheless indicative of negligible bioavailability following exposure via the eyes. Since a chemical is required to be bioavailable in order to induce (non-mechanical) irritation, and since the substance has no pH <2 or >11, palladium dihydroxide is considered incapable of inducing eye corrosion. Therefore, and driven by the inconclusive in vitro data, the registrants consider it justified to not perform further in vivo mammalian testing but instead classify the substance as eye irritant cat 2 (H319).

No respiratory tract irritation data were identified. A new study was not conducted as it is not a REACH Standard Information Requirement. Further, palladium dihydroxide is not expected to reach the lungs in appreciable quantities (based on respiratory tract deposition modelling data - cf section 4.5). Thus, inhalation will not be a significant route of exposure.

Justification for classification or non classification:

Based on the results of the available in vitro skin irritation/corrosion studies with palladium dihydroxide and read-across test data from palladium monoxide, there is no requirement to classify palladium dihydroxide for skin irritation according to EU CLP criteria (EC 1272/2008).

Based on the results of the available in vitro eye irritation studies with palladium dihydroxide, combined with read-across test data from palladium monoxide, the low water solubility of palladium dihydroxide and the low dermal bioaccessibility of palladium dihydroxide, it was considered justified to classify palladium dihydroxide as eye irritant cat 2 (H319) according to EU CLP criteria (EC 1272/2008).



5.4. Corrosivity

5.4.1. Non-human information

The results of studies on skin irritation related to corrosivity are summarised in the following table:

Table 5.4. Studies on skin irritation related to corrosivity

Method	Results	Remarks
Tissue studied: skin corrosion: in vitro / ex vivo Coverage: Vehicle: according to guideline MatTek test protocol "In vitro EpiDerm™ Skin Corrosion Test (EPI-200-SCT)", 07 November 2014. ; according to guideline EU Method B.40 (In Vitro Skin Corrosion: Transcutaneous Electrical Resistance Test (TER)) ; according to guideline OECD Guideline 431 (In Vitro Skin Corrosion: Reconstructed Human Epidermis (RHE) Test Method) [from 26 Sept. 2014]	GHS criteria not met % tissue viability 60 min exposure. Value: 100.75 (no indication of irritation) 3 min exposure. Value: 99.59 (no indication of irritation)	1 (reliable without restriction) key study experimental study Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, (full information in Annex II). Reference Spohr 2021

5.4.2. Human information

No relevant information available.

5.4.3. Summary and discussion of corrosion

Skin irritation / corrosion_PdO_Campbell et al. (1975).source

The studies with results indicating corrosivity are discussed in section 5.3.4 Summary and discussion of irritation.

5.5. Sensitisation

5.5.1. Skin

5.5.1.1. Non-human information

The results of studies on skin sensitisation are summarised in the following table:

Table 5.5. Studies on skin sensitisation

Method	Results	Remarks
mouse (CBA/Ca [mouse] - Mice, CBA/CaOlaHsd, Recognised as the recommended test system. Source: Envigo RMS B.V., Inc Postbus 6174 5960 AD Horst / The Netherlands) female skin sensitisation: in vivo (LLNA) according to guideline EU Method B.42 (Skin Sensitisation: Local Lymph Node Assay) ; according to guideline OECD Guideline 429 (Skin Sensitisation: Local	GHS criteria not met Stimulation index: 1 (no indication of skin sensitisation based on QSAR/QSPR prediction - Stimulation Indices of 1.0, 1.8, and 2.5 were determined with the test item at concentrations of 5, 10 and 25% in propylene glycol. Since these values were all below the threshold value of 3, the EC3 value could not be calculated and the test item is considered to lack the potential to cause skin	1 (reliable without restriction) key study experimental study Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, (full information in Annex II).



Lymph Node Assay)	sensitisation.) Stimulation index: 1.8 (no indication of skin sensitisation based on QSAR/QSPR prediction - Stimulation Indices of 1.0, 1.8, and 2.5 were determined with the test item at concentrations of 5, 10 and 25% in propylene glycol. Since these values were all below the threshold value of 3, the EC3 value could not be calculated and the test item is considered to lack the potential to cause skin sensitisation.) Stimulation index: 2.5 (no indication of skin sensitisation based on QSAR/QSPR prediction - Stimulation Indices of 1.0, 1.8, and 2.5 were determined with the test item at concentrations of 5, 10 and 25% in propylene glycol. Since these values were all below the threshold value of 3, the EC3 value could not be calculated and the test item is considered to lack the potential to cause skin sensitisation.)	Reference Dony 2021
in vitro study skin sensitisation: in vitro according to guideline OECD Guideline 442D (In Vitro Skin Sensitisation: ARE-Nrf2 luciferase KeratinoSens™ test method) [from 25 June 2018]	Palladium dihydroxide did not produce a visually clear solution or a stable dispersion at sufficient concentrations to meet the OECD Test Guideline for ARE-Nrf2 Luciferase Test Method (LuSens).	1 (reliable without restriction) supporting study experimental study Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, (full information in Annex II). Reference Machulla 2020

Data waiving

Information requirement: Skin Sensitisation

Reason: study scientifically not necessary / other information available

Justification: an in vitro skin sensitisation study does not need to be conducted because the available in vitro test methods are not applicable for the substance and therefore an in vivo skin sensitisation study was conducted [study scientifically not necessary / other information available] - The in vitro methods described in OECD 442 C, D & E were found to be unsuitable for use with palladium dihydroxide. OECD442C is not applicable to metals, as specified in the OECD guidance document, and Palladium dihydroxide did not produce a visually clear solution or a stable dispersion at sufficient concentrations to meet the OECD Test Guideline for ARE-Nrf2 Luciferase Test Method (LuSens; Machulla 2020). Therefore, the in vitro test battery could not provide sufficient information for a solid conclusion on the skin sensitising potential.

5.5.1.2. Human information

No relevant information available.



5.5.2. Respiratory system

5.5.2.1. Non-human information

No relevant information available.

5.5.2.2. Human information

No relevant information available.

5.5.3. Summary and discussion of sensitisation

The following information is taken into account for any hazard / risk assessment:

Skin sensitisation

Key Information:

The in vitro methods described in OECD 442 C, D & E were found to be unsuitable for use with palladium dihydroxide.

The Local Lymph Node Assay (OECD 429, GLP compliant) was therefore required to make a prediction of the skin sensitisation potential of the test article. The assay showed no skin sensitising properties.

Palladium dihydroxide is concluded to not exert skin sensitising properties.

Value used for CSA: no adverse effect observed (not sensitising)

Relevant studies: Skin sensitisation.Pd(OH)₂_Dony(2021)

Additional information:

The in vitro methods described in OECD 442 C, D & E were found to be unsuitable for use with palladium dihydroxide. OECD442C is not applicable to metals, as specified in the OECD guidance document, and Palladium dihydroxide did not produce a visually clear solution or a stable dispersion at sufficient concentrations to meet the OECD Test Guideline for ARE-Nrf2 Luciferase Test Method (LuSens). Therefore, the in vitro test battery could not provide sufficient information for a solid conclusion on the skin sensitising potential.

The Local Lymph Node Assay (OECD 429, GLP compliant) was therefore required to make a prediction of the skin sensitisation potential of the test article. The assay showed no skin sensitising properties.

Palladium dihydroxide is concluded to not exert skin sensitising properties.

Justification for selection of skin sensitisation endpoint:

substance specific data generated under GLP with the test item of interest

Respiratory sensitisation

Value used for CSA: no study available

Additional information:

No respiratory tract sensitisation data are available. A new study was not conducted as no standard and validated test method is available and it is not a REACH Standard Information Requirement. Further, the compound is not expected to reach the lungs in appreciable quantities (based on respiratory tract deposition modelling data). Thus, inhalation will not be a significant route of exposure.

Justification for classification or non classification:



Based on the results of the available skin sensitisation studies on palladium dihydroxide, it is concluded that the substance does not meet the classification criteria according to EU CLP criteria (EC 1272/2008).

5.6. Repeated dose toxicity

5.6.1. Non-human information

5.6.1.1. Repeated dose toxicity: oral

The results of studies are summarised in the following table:

Table 5.6. Studies on repeated dose toxicity after oral administration

Method	Results	Remarks
rat [common rodent species] (Wistar [rat]) male/female short-term repeated dose toxicity: oral - combined repeated dose and reproduction / developmental screening (oral: gavage) Vehicle: corn oil Exposure: Male and female Wistar rats were treated for 2 weeks pre-mating and then during the mating/post-mating periods. This was 28 days in total for males. Females were treated throughout gestation and up to and including postpartum/lactation Day 4 (i.e. around 50 days in total). (Test item or negative control treated animals were administered the dosing formulations daily on a 7 days/week basis) according to guideline OECD Guideline 422 (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test)	NOAEL: 1000 mg/kg bw/day (nominal) (male/female based on: (test mat.) behaviour (functional findings) ; body weight and weight gain ; clinical biochemistry ; clinical signs ; food consumption and compound intake ; gross pathology ; haematology ; histopathology: non-neoplastic ; mortality ; organ weights and organ / body weight ratios ; urinalysis	1 (reliable without restriction) key study experimental study Test material palladium(2+) dihydroxide / 12135- 22-7 / 235-219-2, Form: solid: particulate/powder - migrated information: powder (full information in Annex II). Reference Török-Bathó M 2015

5.6.1.2. Repeated dose toxicity: inhalation

No relevant information available.

5.6.1.3. Repeated dose toxicity: dermal

No relevant information available.

5.6.1.4. Repeated dose toxicity: other routes

No relevant information available.

5.6.2. Human information

No relevant information available.

5.6.3. Summary and discussion of repeated dose toxicity



The following information is taken into account for any hazard / risk assessment:

Key Information:

In an OECD Test Guideline 422 combined repeated dose and reproductive/developmental toxicity screening study in rats, involving the gavage administration of palladium dihydroxide for at least 28 days, the systemic NOAEL was the highest tested dose (1000 mg/kg bw/day).

Although some treatment related microscopic findings (mucosal discoloration in the non-glandular stomach, ileum, cecum, colon and/or rectum) were noted at dose levels of 300 and 1000 mg/kg bw/day, these were considered to result from direct (local) contact with the test substance rather than systemic toxicity (Török-Bathó, 2015).

No repeated dose toxicity studies by the inhalation or dermal route were identified, or are required.

Value used for CSA (via oral route - systemic effects):

no adverse effect observed

(NOAEL: 1000mg/kg bw/day; subacute, rat [common rodent species])

Relevant studies: Repeated dose toxicity: oral (KEY)_Pd dihydroxide_Török-Bathó (2015)

Value used for CSA (inhalation - systemic effects):

no study available

Value used for CSA (inhalation - local effects):

no study available

Value used for CSA (dermal - systemic effects):

no study available

Value used for CSA (dermal - local effects):

no study available

Additional information:

No relevant human data were identified.

In a combined repeated dose toxicity and reproductive/developmental toxicity screening study, conducted according to OECD Test Guideline 422 and to GLP, rats were orally administered palladium dichloride by stomach tube (gavage) at about 0, 100, 300 or 1000 mg/kg bw/day. Male and female Wistar rats (12 animals/sex/group) were treated for 2 weeks pre-mating and then during the mating/post-mating periods. This was 28 days in total for males. Females were also treated throughout gestation and up to and including postpartum/lactation Day 4 (i.e. around 50 days in total). Daily administration of palladium dihydroxide by oral gavage to Wistar rats did not result in test item related mortality or clinical adverse effects at daily, weekly or neurological assessment, or changes in the body weight, food consumption, haematology, coagulation, clinical chemistry, or urinalysis parameters at dose levels of up to 1000 mg/kg bw/day during the treatment period. There were no adverse treatment-related changes in organ weights for the adult animals of either sex. There were no changes observed at histopathology considered indicative of treatment-related systemic toxicity. Test item-related black discoloration of the digestive contents or brown mucosal discoloration in the non-glandular stomach, ileum, caecum, colon and/or rectum at necropsy, corresponded with black granular foreign material noted by light microscopy. These changes were considered to result from direct contact with the test item (i.e. local effects) and not to systemic toxicity. In conclusion, in this guideline GLP study, the systemic no-observed-adverse-effect level (NOAEL) of palladium dihydroxide was 1000 mg/kg bw/day (Török-Bathó, 2015). The oral NOAEL for palladium dihydroxide (1000 mg/kg bw/day) equates to an NOAEL of 758 mg/kg bw/day for palladium (based on MWt ratio).

According to REACH Annex VIII (EC 1907/2006), repeated dose toxicity studies only need to be conducted on one species taking into consideration the most appropriate route of administration regarding human exposure. The compound is not expected to reach the lungs in appreciable quantities (based on respiratory tract deposition modelling data). Thus, inhalation will not be a significant route of exposure. Similarly, skin contact during production and/or use is expected to be negligible. As the oral route of exposure is considered the most appropriate, repeated dose toxicity studies were not carried out for the dermal or inhalation routes.



Justification for selection of repeated dose toxicity via oral route - systemic effects endpoint:
GLP study, conducted according to OECD guidelines, and the only repeated dose toxicity study available.

Justification for classification or non classification:

No adverse systemic effects were seen in a reliable repeated dose toxicity study (combined with a reproductive/developmental screening assay) following gavage administration of rats for at least 28 days. As such, classification of palladium dihydroxide as STOT-RE is not required, according to EU CLP criteria (EC 1272/2008).

Detailed information on the Mode of Action is available in **Annex III**.

5.7. Mutagenicity

5.7.1. Non-human information

5.7.1.1. In vitro data

The results of in vitro genotoxicity studies are summarised in the following table:

Table 5.7. In vitro genotoxicity studies:

Method	Results	Remarks
<p>in vitro mammalian cell micronucleus test [in vitro cytogenicity / micronucleus study] (in vitro cytogenicity / micronucleus study)</p> <p>lymphocytes isolated from whole blood of a non-smoking volunteer (18-35) - The details of the donors used are: -Preliminary Toxicity Test: male, aged 30 years -Main Experiment: male, aged 31 years (with and without met. act.)</p> <p>Test concentrations: Preliminary Toxicity Test Three exposure groups were used: i) 4-hour exposure to the test item without S9-mix, followed by a 24 hour incubation period in treatment-free media, in the presence of Cytochalasin B, prior to cell harvest. ii) 4-hour exposure to the test item with S9-mix (2%), followed by a 24 hour incubation period in treatment-free media, in the presence of Cytochalasin B, prior to cell harvest. iii) 24-hour continuous exposure to the test item without S9-mix, followed by a 24 hour incubation period in treatment-free media, in the presence of Cytochalasin B, prior to cell harvest. The dose levels of test item used were 0, 5.48, 10.97, 21.94, 43.88, 87.75, 175.5, 351, 702, and 1404 µg/mL. The maximum dose was the 10 mM limit dose level. A precipitate of the test item was observed in the parallel blood-free cultures at the end of the exposure at and above 87.75µg/mL in all three of the exposure groups. Parallel flasks, containing culture medium without whole blood, were established for the three</p>	<p>Test results: negative for lymphocytes; met. act.: with and without genotoxicity: negative cytotoxicity: no cytotoxicity, but tested up to precipitating concentrations vehicle controls valid: valid negative controls valid: not applicable positive controls valid: valid</p>	<p>1 (reliable without restriction) key study experimental study</p> <p>Test material palladium(2+) dihydroxide / 12135- 22-7 / 235-219-2, (full information in Annex II).</p> <p>Reference Willey 2021</p>



<p>exposure conditions so that test item precipitate observations could be made. Precipitate observations were recorded at the beginning and end of the exposure periods. Using a qualitative microscopic evaluation of the microscope slide preparations from each treatment culture, appropriate dose levels were selected for the evaluation of the frequency of binucleate cells and to calculate the cytokinesis block proliferation index (CBPI). Coded slides were evaluated for the CBPI. The CBPI data were used to estimate test item toxicity and for selection of the dose levels for the exposure groups of the main experiment. For the Main Experiment, the dose levels of test item used were 0, 2.74, 5.48, 10.97, 21.94, 43.88, 87.75, and 175.5 µg/mL. Precipitate observations were recorded at the beginning and end of the exposure periods.</p> <p>Positive control substance(s): cyclophosphamide - 5 µg/mL for 4-hour exposure (+S9) ; mitomycin C - 0.2 µg/mL for 4-hour exposure (-S9) ; demecolcine - 0.075 µg/mL for 24-hour continuous exposure (-S9) according to guideline OECD Guideline 487 (In vitro Mammalian Cell Micronucleus Test) [in vitro cytogenicity / micronucleus study]</p>		
<p>bacterial reverse mutation assay [in vitro gene mutation study in bacteria] (in vitro gene mutation study in bacteria)</p> <p>S. typhimurium TA 1535, TA 1537, TA 98, TA 100 and E. coli WP2 [bacteria] - The bacteria used in the test were obtained from: • British Industrial Biological Research Association, on a nutrient agar plate, on 17 August 1987 • Trinova Biochem GmbH on 27 June 2017. (with and without met. act.)</p> <p>Test concentrations: Exp1: The maximum concentration was 5000 µg/plate (the OECD TG 471 maximum recommended dose level). Eight concentrations of the test item (1.5, 5, 15, 50, 150, 500, 1500 and 5000 µg/plate) were assayed in triplicate against each tester strain, using the direct plate incorporation method.</p> <p>Exp2: As the result of Experiment 1 was considered negative, Experiment 2 was performed using the pre-incubation method in the presence and absence of metabolic activation (S9-mix). The dose range used for Experiment 2 was</p>	<p>Test results: negative for E. coli WP2 uvr A [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity vehicle controls valid: valid negative controls valid: valid positive controls valid: valid</p> <p>Test results: negative for S. typhimurium TA 100 [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity vehicle controls valid: valid negative controls valid: valid positive controls valid: valid</p> <p>Test results: negative for S. typhimurium TA 98 [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity vehicle controls valid: valid</p>	<p>1 (reliable without restriction) key study experimental study</p> <p>Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, (full information in Annex II).</p> <p>Reference Wisher 2021</p>



<p>determined by the results of Experiment 1 and was 0.5, 1.5, 5, 15, 50, 150, 500 and 1500 µg/plate. Eight test item concentrations were selected in Experiment 2 in order to ensure the study achieved at least four non-toxic dose levels as required by the test guideline, and were selected based on the cytotoxicity noted in Experiment 1 and the potential for a change in the cytotoxicity of the test item following the change in test methodology from plate incorporation to pre-incubation.</p> <p>Positive control substance(s): 4-nitroquinoline-N-oxide ; 9-aminoacridine ; N-ethyl-N-nitro-N-nitrosoguanidine ; benzo(a)pyrene ; according to guideline ICH S2(R1) guideline adopted June 2012 (ICH S2(R1) Federal Register. Adopted 2012; 77:33748-33749) ; according to guideline JAPAN: Guidelines for Screening Mutagenicity Testing Of Chemicals [genetic toxicity in vitro, other] ; according to guideline EPA OPPTS 870.5100 - Bacterial Reverse Mutation Test (August 1998) [in vitro gene mutation study in bacteria] ; according to guideline EU Method B.13/14 (Mutagenicity - Reverse Mutation Test Using Bacteria) [in vitro gene mutation study in bacteria] ; according to guideline OECD Guideline 471 (Bacterial Reverse Mutation Assay) [in vitro gene mutation study in bacteria]</p>	<p>negative controls valid: valid positive controls valid: valid</p> <p>Test results: negative for <i>S. typhimurium</i> TA 1537 [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity vehicle controls valid: valid negative controls valid: valid positive controls valid: valid</p> <p>Test results: negative for <i>S. typhimurium</i> TA 1535 [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity vehicle controls valid: valid negative controls valid: valid positive controls valid: valid</p>	
<p>in vitro mammalian cell gene mutation test using the Hprt and xprt genes [in vitro gene mutation study in mammalian cells] (in vitro gene mutation study in mammalian cells)</p> <p>V79 cell line (with and without met. act.)</p> <p>Test concentrations: The molecular weight of the test item was 140.43 therefore the maximum proposed dose level in the solubility test was set at 1404.3 µg/mL, the 10 mM limit dose level and a correction for the purity of the test item of 97.4% was applied to the formulations. The test item formed a suspension in MEM suitable for dosing at 14.04 mg/mL and was therefore selected as the solvent. There was no significant change in pH when the test item was dosed into media and the osmolality did not increase by more than 50 mOsm at the concentration levels investigated (Scott et al., 1991). A dose range of 0, 5.49, 10.97,</p>	<p>Test results: negative for Chinese hamster lung fibroblasts (V79) [mammalian cell line]; met. act.: with and without genotoxicity: negative cytotoxicity: no cytotoxicity, but tested up to precipitating concentrations vehicle controls valid: valid negative controls valid: positive controls valid: valid</p>	<p>1 (reliable without restriction) key study experimental study</p> <p>Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, Form: solid: particulate/powder - migrated information: powder (full information in Annex II).</p> <p>Reference Morris 2021</p>



<p>21.94, 43.88, 87.77, 175.54, 351.08, 702.15, and 1404.3 µg/mL was used in the preliminary cytotoxicity test. The maximum dose tested was the 10mM limit concentration of 1404.3 µg/mL. A precipitate of the test item was observed at the end of exposure at and above 87.77 µg/mL in both of the exposure groups.</p> <p>Main experiment: The dose levels of the test item (4-h -/+S9): 0-5.5-11-22-44-88-176-352 µg Pd(OH)₂/L At the end of the exposure period, precipitate of the test item was observed at and above 88 µg/mL in both the absence and presence of metabolic activation. Therefore, the lowest precipitating dose level was plated for relative survival growth and expression of induced mutants, as recommended by the OECD 476 guideline, and the subsequent dose levels were discarded as they were considered surplus to requirements. No analysis was conducted to determine the homogeneity, concentration or stability of the test item formulation. The test item was formulated within two hours of it being applied to the test system; it is assumed that the formulation was stable for this duration.</p> <p>Positive control substance(s): ethylmethanesulphonate ; dimethyl benzanthracene (DMBA)</p> <p>according to guideline EPA OPPTS 870.5300 - In vitro Mammalian Cell Gene Mutation Test [in vitro gene mutation study in mammalian cells] ; according to guideline EU Method B.17 (Mutagenicity - In Vitro Mammalian Cell Gene Mutation Test) [in vitro gene mutation study in mammalian cells] ; according to guideline OECD Guideline 476 (In Vitro Mammalian Cell Gene Mutation Test using the Hprt and xpRT genes) [in vitro gene mutation study in mammalian cells (from 28 July 2015)]</p>		
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5.7.1.2. In vivo data

No relevant information available.

5.7.2. Human information

No relevant information available.

5.7.3. Summary and discussion of mutagenicity

The following information is taken into account for any hazard / risk assessment (genetic toxicity in vitro):



In a Reverse Mutation Assay 'Ames Test' using strains of *Salmonella typhimurium* and *Escherichia coli* (OECD TG 471, GLP compliant) the test item Palladium dihydroxide did not induce an increase in the frequency of revertant colonies that met the criteria for a positive result, either with or without metabolic activation (S9-mix). Under the conditions of this test Palladium dihydroxide was considered to be non-mutagenic when tested up to the limit of toxicity.

Palladium dihydroxide was considered to be non-clastogenic and non-aneugenic to human lymphocytes in vitro (test according to OECD487). The test item did not induce any statistically significant increases in the frequency of binucleate cells with micronuclei in either the absence or presence of a metabolizing system. The test item was therefore considered to be non-clastogenic and non-aneugenic to human lymphocytes in vitro when tested to its lowest precipitating dose level.

Palladium dihydroxide did not induce any toxicologically significant or concentration-related increases in mutant frequency per survivor in either the absence or presence of metabolic activation and was shown to be non-mutagenic to V79 cells at the HPRT locus under the conditions of the test.

Value used for CSA (genetic toxicity in vitro): Genetic toxicity: no adverse effect observed (negative)

The following information is taken into account for any hazard / risk assessment (genetic toxicity in vivo):
No in vivo data were identified.

Value used for CSA (genetic toxicity in vivo): Genetic toxicity: no study available

Justification for classification or non classification

Based on the existing data set, palladium dihydroxide does not meet the criteria for classification as a germ cell mutagen (category 1A/B or 2) under EU CLP criteria (EC 1272/2008).

Relevant studies: Genetic toxicity in vitro.Pd(OH)₂_AMES_Wisher(2021)

Relevant studies: Genetic toxicity in vitro.Pd(OH)₂_hprt_Morris(2021)

Relevant studies: Genetic toxicity in vitro.Pd(OH)₂_IVMN_Willey(2021)

Additional information:

In vitro test data with palladium dihydroxide were available. In a Reverse Mutation Assay 'Ames Test' using strains of *Salmonella typhimurium* and *Escherichia coli* (OECD TG 471, GLP compliant) the test item Palladium dihydroxide did not induce an increase in the frequency of revertant colonies that met the criteria for a positive result, either with or without metabolic activation (S9-mix). Under the conditions of this test Palladium dihydroxide was considered to be non-mutagenic when tested up to the limit of toxicity. Palladium dihydroxide was considered to be non-clastogenic and non-aneugenic to human lymphocytes in vitro (test according to OECD487). The test item did not induce any statistically significant increases in the frequency of binucleate cells with micronuclei in either the absence or presence of a metabolizing system. The test item was therefore considered to be non-clastogenic and non-aneugenic to human lymphocytes in vitro when tested to its lowest precipitating dose level. Palladium dihydroxide did not induce any toxicologically significant or concentration-related increases in mutant frequency per survivor in either the absence or presence of metabolic activation and was shown to be non-mutagenic to V79 cells at the HPRT locus under the conditions of the test.

No in vivo data were identified.

Several Expert Groups have assessed the toxicity profile of palladium, and various palladium compounds, including the assessment of CMR properties. The overwhelming weight-of-evidence (including good-quality in vitro and in vivo studies) indicates that palladium and palladium compounds are of no concern for mutagenic activity (bibra, 2007; DFG, 2006; EFSA, 2012, 2014; WHO, 2002). In addition, proprietary genotoxicity studies (including in vitro bacterial and mammalian studies assessing mutagenicity and clastogenicity, and an in vivo micronucleus study) of palladium compounds were overwhelmingly negative.

Justification for selection of genetic toxicity endpoint

GLP studies, conducted according to OECD guidelines.

Detailed information on the Mode of Action is available in **Annex III**.



5.8. Carcinogenicity

5.8.1. Non-human information

5.8.1.1. Carcinogenicity: oral

No relevant information available.

5.8.1.2. Carcinogenicity: inhalation

No relevant information available.

5.8.1.3. Carcinogenicity: dermal

No relevant information available.

5.8.1.4. Carcinogenicity: other routes

No relevant information available.

5.8.2. Human information

No relevant information available.

5.8.3. Summary and discussion of carcinogenicity

5.9. Toxicity for reproduction

5.9.1. Effects on fertility

5.9.1.1. Non-human information

The results of studies on fertility are summarised in the following table:

Table 5.8. Studies on fertility

Method	Results	Remarks
rat (Wistar [rat]) male/female screening for reproductive / developmental toxicity - based on test type (migrated information) oral: gavage Doses / Concentrations: 0, 100, 300, 1000 mg/kg bw/day Basis: nominal conc. Vehicle: corn oil Exposure: Male and female Wistar rats were treated for 2 weeks pre-mating and then during the mating/post-mating periods. This was 28 days in total for males. Females were treated throughout gestation and up to and including postpartum/lactation Day 4 (Test item or negative control treated animals were administered the dosing formulations daily on a 7 days/week basis)	First parental generation (P0) NOAEL (PO) 1000 mg/kg bw/day (nominal) (male/female) based on: clinical signs [general toxicity] ; body weight and weight gain [general toxicity] ; food consumption and compound intake [general toxicity] ; organ weights and organ / body weight ratios [general toxicity] ; gross pathology [general toxicity] ; histopathology: non-neoplastic [general toxicity] ; reproductive performance [reproductive toxicity] F1 generation NOAEL : 1000 mg/kg bw/day (nominal) (male/female) based on: viability ; clinical signs ; gross pathology ; developmental effects Overall reproductive toxicity	1 (reliable without restriction) key study experimental study Test material palladium(2+) dihydroxide / 12135- 22-7 / 235-219-2, Form: solid: particulate/powder - migrated information: powder (full information in Annex II). Reference Török-Bathó M 2015



according to guideline OECD Guideline 422 (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test)	not specified Lowest effective dose / concentration Relation to other toxic effects:	
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Toxicity to reproduction: other studies

No relevant information available.

5.9.1.2. Human information

No relevant information available.

5.9.2. Developmental toxicity**5.9.2.1. Non-human information**

The results of studies on developmental toxicity are summarised in the following table:

Table 5.9. Studies on developmental toxicity

Method	Results	Remarks
rat (Wistar [rat]) oral: gavage Vehicle: corn oil Exposure: Male and female Wistar rats were treated for 2 weeks pre-mating and then during the mating/post-mating periods. This was 28 days in total for males. Females were treated throughout gestation and up to and including postpartum/lactation Day 4 (Test item or negative control treated animals were administered the dosing formulations daily on a 7 days/week basis) according to guideline OECD Guideline 422 (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test)	Maternal animals: NOAEL: 1000 mg/kg bw/day (nominal) based on: (test mat.) Fetuses: NOAEL: 1000 mg/kg bw/day (nominal) based on: (test mat.) Overall developmental toxicity: no Lowest effective dose / concentration: Relation to maternal toxicity:	1 (reliable without restriction) key study experimental study Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, Form: solid: particulate/powder - migrated information: powder (full information in Annex II). Reference Török-Bathó M 2015

5.9.2.2. Human information

No relevant information available.

5.9.3. Summary and discussion of reproductive toxicity**Effects on fertility**

The following information is taken into account for any hazard / risk assessment:

In an OECD Test Guideline 422 combined repeated dose and reproductive/developmental toxicity screening study in rats, involving the gavage administration of palladium dihydroxide, the systemic and reproductive NOAEL was the highest tested dose (1000 mg/kg bw/day) (Török-Bathó, 2015).



Value used for CSA (route: oral):

no adverse effect observed (NOAEL): 1000mg/kg bw/day (subacute, rat [common rodent species])

Relevant studies: Toxicity to reproduction (KEY)_Pd dihydroxide_Török-Bathó (2015)

Relevant studies: Developmental toxicity / teratogenicity (KEY)_Pd dihydroxide_Török-Bathó (2015)

Value used for CSA (route: dermal):

no study available

Value used for CSA (route: inhalation):

no study available

Additional information:

No relevant data in humans were identified.

In a combined repeated dose toxicity and reproductive/developmental toxicity screening study, conducted according to OECD Test Guideline 422 and to GLP, rats were orally administered palladium dihydroxide by stomach tube (gavage) at about 0, 100, 300 or 1000 mg/kg bw/day. Male and female Wistar rats (12 animals/sex/group) were treated for 2 weeks pre-mating and then during the mating/post-mating periods. This was 28 days in total for males. Females were also treated throughout gestation and up to and including postpartum/lactation Day 4 (i.e. around 50 days in total). No test-item related adverse effects on reproductive performance (notably mating and fertility indices, and gestation index), oestrous cyclicity or sperm parameters, were observed. The numbers of implantation sites and corpora lutea were also unaffected by treatment. No treatment-related effect on the weight, gross appearance or microscopic examination of the reproductive organs was reported. In conclusion, under the conditions of this study, the systemic and reproductive toxicity NOAEL of palladium dihydroxide was 1000 mg/kg bw/day (the highest tested dose) (Török-Bathó, 2015).

No reproductive toxicity studies by the inhalation or dermal route were identified, or are required.

Justification for selection of Effect on fertility via oral route:

GLP study, conducted according to OECD guidelines, and the only reproduction toxicity study available.

Developmental toxicity

The following information is taken into account for any hazard / risk assessment:

In an OECD Test Guideline 422 combined repeated dose and reproductive/developmental toxicity screening study in rats, involving the gavage administration of palladium dihydroxide, the systemic and developmental toxicity NOAEL was the highest tested dose (1000 mg/kg bw/day) (Török-Bathó, 2015).

Effect on developmental toxicity - development (via oral route)

Value used for CSA (route: oral):

no adverse effect observed (NOAEL): 1000mg/kg bw/day (subacute; rat [common rodent species])

Relevant studies: Toxicity to reproduction (KEY)_Pd dihydroxide_Török-Bathó (2015)

Relevant studies: Developmental toxicity / teratogenicity (KEY)_Pd dihydroxide_Török-Bathó (2015)

Effect on developmental toxicity - development (via dermal route)

Value used for CSA (route: dermal):

no study available

Effect on developmental toxicity - development (via inhalation route)

Value used for CSA (route: inhalation):

no study available

Additional information:



No relevant data in humans were identified.

In a combined repeated dose toxicity and reproductive/developmental toxicity screening study, conducted according to OECD Test Guideline 422 and to GLP, rats were orally administered palladium dihydroxide by stomach tube (gavage) at about 0, 100, 300 or 1000 mg/kg bw/day. Male and female Wistar rats (12 animals/sex/group) were treated for 2 weeks pre-mating and then during the mating/post-mating periods. This was 28 days in total for males. Females were also treated throughout gestation and up to and including postpartum/lactation Day 4 (i.e. around 50 days in total). No maternal systemic toxicity was observed, and the numbers of implantation sites and corpora lutea were unaffected by treatment. The F1 offspring were assessed for number and sex of pups, stillbirths, live births, runts (pups that are apparently smaller than normal pups), and to detect the presence of gross abnormalities. A number of offspring viability and sex ratio indices were calculated (including survival index, pre-implantation and intrauterine mortality, and sex ratio of males). In addition, pups were monitored for any behavioural changes. Live pups were counted, sexed and weighed individually within 24 hours of parturition (post-natal day (PND)0 or PND1) and on PND4. All the litters were checked daily for the numbers of viable and dead pups. Dead pups and pups euthanized at PND4 were examined externally for gross abnormalities. Dead pups were necropsied with macroscopic examination in order to identify the probable cause of death. No foetal toxicity or developmental effects were reported. In conclusion, under the conditions of this study, no treatment-related effects on maternal/foetal toxicity, or developmental effects, were seen resulting in a systemic and developmental toxicity NOAEL for palladium dihydroxide of 1000 mg/kg bw/day (the highest tested dose) (Török-Bathó, 2015).

No developmental toxicity studies by the inhalation or dermal route were identified, or are required.

Justification for selection of Effect on developmental toxicity: via oral route:

GLP study, conducted according to OECD guidelines, and the only reproduction/developmental toxicity study available.

Justification for classification or non classification:

No adverse effects on reproductive parameters (sexual function or fertility) or development of offspring were seen in a reliable guideline combined repeated dose toxicity study and reproductive/developmental toxicity screening study with palladium dihydroxide. As such, classification for reproductive/developmental toxicity is not required, according to EU CLP criteria (EC 1272/2008).

Detailed information on the Mode of Action is available in **Annex III**.

5.10. Other effects

5.10.1. Non-human information

5.10.1.1. Neurotoxicity

No relevant information available.

5.10.1.2. Immunotoxicity

No relevant information available.

5.10.1.3. Specific investigations: other studies

No relevant information available.

5.10.1.4. Additional toxicological effects

The results of specific investigations (other studies) are summarised in the following table:

Table 5.10. Specific investigations: other studies

Method	Results	Remarks
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<p>Study type: according to guideline Standard Operating Procedure (SOP) prepared by Eurometaux on November 2010</p> <p>A bio-accessibility testing study has been designed to assay the metal release of Palladium dihydroxide compounds in gastric synthetic media. Metals or metallic compounds are subjected to a media that mimic gastric juice, in terms of pH and body temperature (pH 1.5 and 37 °C), for an exposure time of 1 hour with agitation. Then the compounds are incubated for another hour without agitation, before aliquots are taken, filtered and bio-accessible metal quantified by ICP-MS.</p>	<p>Applicant's summary and conclusion: Palladium dihydroxide showed solubility of 77.8 n% after 2 hours in gastric juice. After incubation in gastric juice, 103625 µg/L of Pd (507970 µg/g) was released from samples after 2 hours.</p>	<p>1 (reliable without restriction) key study experimental study</p> <p>Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, Form: not specified (full information in Annex II).</p> <p>Reference Brouwers T 2017</p>
<p>Study type: according to guideline Standard Operating Procedure (SOP) prepared by Eurometaux on November 2010</p> <p>A bio-accessibility testing study has been designed to assay the metal release of Palladium compounds in perspiration synthetic media. Metals or metallic compounds are subjected to a media that mimic perspiration for 7 days at 30 °C and without agitation. Samples are taken at 24 hours and 168 hours of incubation, filtered and the bio-accessible metal quantified by ICP-MS.</p>	<p>Applicant's summary and conclusion: Palladium dihydroxide showed solubility of 2.6 % after 168 hours in perspiration fluid. After incubation in perspiration mimetic fluid, 13673.67 and 34086.67 µg/L (6825.46 and 16992.36 µg/g) of Palladium was released after 24 and 168 hours, respectively.</p>	<p>1 (reliable without restriction) key study experimental study</p> <p>Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, Form: not specified (full information in Annex II).</p> <p>Reference Brouwers T 2017</p>

5.10.2. Human information

No relevant information available.

5.10.3. Summary and discussion of other effects

5.11. Derivation of DNEL(s) and other hazard conclusions

5.11.1. Overview of typical dose descriptors for all endpoints

Table 5.11. Available dose-descriptor(s) per endpoint as a result of its hazard assessment

Endpoint	Route	Dose descriptor or qualitative effect characterisation; test type
Acute toxicity	oral	no adverse effect observed
Acute toxicity	dermal	no study available
Acute toxicity	inhalation	no study available
Irritation / Corrosivity	skin	no adverse effect observed (not irritating)



Irritation / Corrosivity	eye	adverse effect observed (irritating)
Irritation / Corrosivity	resp. tract	no study available
Sensitisation	skin	no adverse effect observed (not sensitising)
Sensitisation	resp. tract	no study available
Repeated dose toxicity	oral	no adverse effect observed (NOAEL): 1000mg/kg bw/day (subacute; rat [common rodent species])
Repeated dose toxicity	dermal (systemic effects)	no study available
Repeated dose toxicity	dermal (local effects)	no study available
Repeated dose toxicity	inhalation (systemic effects)	no study available
Repeated dose toxicity	inhalation (local effects)	no study available
Mutagenicity	in vitro / in vivo	In vitro: no adverse effect observed (negative) In vivo: no study available
Reproductive toxicity: effects on fertility	oral	no adverse effect observed (NOAEL): 1000mg/kg bw/day (subacute; rat [common rodent species])
Reproductive toxicity: effects on fertility	dermal	no study available
Reproductive toxicity: effects on fertility	inhalation	no study available
Reproductive toxicity: developmental toxicity	oral	no adverse effect observed (NOAEL): 1000mg/kg bw/day (subacute; rat [common rodent species])
Reproductive toxicity: developmental toxicity	dermal	no study available
Reproductive toxicity: developmental toxicity	inhalation	no study available

5.11.2. Selection of the DNEL(s) or other hazard conclusions for critical health effects

Table 5.12. Hazard conclusions for workers

Route	Type of effect	Hazard conclusion	Most sensitive endpoint
Inhalation	Systemic effects - Long-term	no hazard identified	
Inhalation	Systemic effects - Acute	no hazard identified	



Inhalation	Local effects - Long-term	no hazard identified	
Inhalation	Local effects - Acute	no hazard identified	
Dermal	Systemic effects - Long-term	no hazard identified	
Dermal	Systemic effects - Acute	no hazard identified	
Dermal	Local effects - Long-term	no hazard identified	
Dermal	Local effects - Acute	no hazard identified	
Eyes	Local effects	medium hazard (no threshold derived)	

Table 5.13. Hazard conclusions for the general population

Route	Type of effect	Hazard conclusion	Most sensitive endpoint
Inhalation	Systemic effects - Long-term	no hazard identified	
Inhalation	Systemic effects - Acute	no hazard identified	
Inhalation	Local effects - Long-term	no hazard identified	
Inhalation	Local effects - Acute	no hazard identified	
Dermal	Systemic effects - Long-term	no hazard identified	
Dermal	Systemic effects - Acute	no hazard identified	
Dermal	Local effects - Long-term	no hazard identified	
Dermal	Local effects - Acute	no hazard identified	
Oral	Systemic effects - Long-term	no hazard identified	
Oral	Systemic effects - Acute	no hazard identified	



Eyes	Local effects	medium hazard (no threshold derived)	
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Discussion:

During assessment of the identified uses for palladium dihydroxide, no uses have been identified in which consumers are exposed to palladium dihydroxide. In all uses with potential consumer exposure due to service life of articles, palladium dihydroxide is chemically transformed into another substance before reaching the consumers, and the subsequent lifecycle steps after this transformation of palladium dihydroxide are appropriately included in the assessment of this newly formed substance. Regarding the general population, and following the criteria outlined in ECHA guidance R16 (2016), an assessment of indirect exposure of humans via the environment for palladium dihydroxide has not been performed as the registered substance is manufactured/imported/marketed <100 tpa and is not classified as STOT-RE 1 or as CMR.



6. HUMAN HEALTH HAZARD ASSESSMENT OF PHYSICOCHEMICAL PROPERTIES

6.1. Explosivity

No relevant information available.

Data waiving: see CSR section 1.3 Physicochemical properties.

Classification according to GHS

Name: Palladium dihydroxide

Related composition: Palladium dihydroxide (solid and powder)

Classification: data conclusive but not sufficient for classification

6.2. Flammability

Flammability

The available information on flammability is summarised in the following table:

Table 6.1. Information on flammability

Method	Results	Remarks
flammable solids equivalent or similar to guideline EC No 1272/2008 Method N.1 of the United Nations Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria, fifth revised edition 2009	Evaluation of results: non flammable - Migrated information Study results: Flammable gasses (lower and upper explosion limits): Aerosols: Flammable solids: burning rate test: preliminary screening test (Pile failed to ignite during the two minutes that the Bunsen flame was applied.) Pyrophoric solids: Pyrophoric liquid: Self-heating substances/mixtures: Substances/ mixture which in contact with water emit flammable gases: Remarks: Pile failed to ignite during the two minutes that the Bunsen flame was applied.	1 (reliable without restriction) key study experimental study Test material palladium(2+) dihydroxide / 12135-22-7 / 235-219-2, (full information in Annex II). Reference Walker JA, White DF 2011

Data waiving: see CSR section 1.3 Physicochemical properties.

Discussion

The following information is taken into account for any hazard / risk assessment:

Flammability

Key value for chemical safety assessment: Flammability: non flammable

Palladium dihydroxide is not classified as a readily combustible solid under Division 4.1 as it failed to ignite in the preliminary screening test.

**Additional information:**

Walker and White (2011) is a GLP compliant, guideline study considered suitable for use as the key study for this endpoint. Palladium dihydroxide is not classified as a readily combustible solid under Division 4.1 as it failed to ignite in the preliminary screening test.

Flash Point

No relevant information available.

Data waiving: see CSR section 1.3 Physicochemical properties.

Classification according to GHS

Name: Palladium dihydroxide

Related composition: Palladium dihydroxide (solid and powder)

Classification (gas): data conclusive but not sufficient for classification

Classification (liquid): data conclusive but not sufficient for classification

Classification (solid): data conclusive but not sufficient for classification

Justification for classification or non-classification:

Based on a GLP-compliant, guideline experimental study palladium dihydroxide is not classified as a readily combustible solid under Division 4.1.

6.3. Oxidising potential

The available information on the oxidising potential is summarised in the following table:

Table 6.2. Information on oxidising potential

Method	Results	Remarks
oxidising solids Contact with: powdered cellulose (>180 s) according to guideline UN Manual of Tests and Criteria: Test O.1 (Test for oxidizing solids)	Evaluation of results: Category 3 (oxidising solids) based on GHS criteria Test results: Oxidising solids: 1:1 sample-to-cellulose ratio: mean burning time: 108 s (burn-off without flames) 4:1 sample-to-cellulose ratio: mean burning time: 73 s (burn-off without flames) Remarks: The sample was a powder according to the sieve analysis 26% of the particles were smaller than 500 µm. The sample was ground for 5 minutes. After grinding, 98% of the particles are smaller than 500 µm. The ground sample was used. Reference mixtures (ratio of potassium to cellulose (by mass): 3:7* - mean burning time (n=5) 129 s (burn- off with flames)	1 (reliable without restriction) key study experimental study Test material palladium(2+) dihydroxide / 12135- 22-7 / 235-219-2, Form: solid: particulate/powder - migrated information: powder (full information in Annex II). Reference Michael-Schulz 2020



	2:3* - mean burning time (n=5) 53s (burn off with flames) *based on the fast burning times of the sample-to-cellulose mixture (4:1) no testing of other reference mixtures was necessary	
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Discussion

The following information is taken into account for any hazard / risk assessment:

Key Information:

Palladium dihydroxide is tested for oxidising properties using UN-Test O.1. Comparing the mean burning times of the sample mixtures with cellulose (t1 and t2) with the mean burning time of the reference mixture (R1), t1 or t2 are <R1. Therefore, it is concluded that palladium dihydroxide fulfils the classification criteria of Division 5.1 "Oxidizing substances", Packing group III, according to the Transport classification or hazard class 'oxidising solids', category 3, according to CLP.

Value used for CSA:

Oxidising properties: oxidising

Relevant studies: Oxidising properties.Key Study - Michael-Schulz 2020

Classification according to GHS

Name: Palladium dihydroxide

Related composition: Palladium dihydroxide (solid and powder)

Classification (gas): data conclusive but not sufficient for classification

Classification (liquid): data conclusive but not sufficient for classification

Classification (solid): Oxid. Solid 3 (Hazard statement: H272: May intensify fire; oxidiser.)

Justification for classification or non-classification:

Palladium dihydroxide fulfils the classification criteria of Division 5.1 "Oxidizing substances", Packing group III, according to the Transport classification or hazard class 'oxidising solids', category 3, according to CLP.



7. ENVIRONMENTAL HAZARD ASSESSMENT

7.1. Aquatic compartment (including sediment)

7.1.1. Fish

7.1.1.1. Short-term toxicity to fish

No relevant information available.

Data waiving

Information requirement: Short-term toxicity testing on fish

Reason: study scientifically not necessary / other information available

Justification: the study does not need to be conducted because the substance is highly insoluble in water, hence indicating that aquatic toxicity is unlikely to occur [study scientifically not necessary / other information available]

Discussion

The following information is taken into account for acute fish toxicity for the derivation of PNEC:

Key Information:

No experimental study is required for palladium dihydroxide based on the outcome of a full TDp assay (cfr. IUCLID Section 4 'Water solubility') and the identified acute and chronic threshold values with other water soluble palladium substances.

The lowest EC50 for acute fish toxicity was determined at >30 µg Pd/L. This is the lowest acute threshold for this endpoint identified with palladium substances, but the study suffered from methodological issues. The lowest threshold identified with reliable studies is 154 µg Pd/L (cfr Environmental Read Across Justification document in IUCLID Section 13 for more details).

Freshwater fish

Dose descriptor: EC50

Effect concentration: 30 µg/L

Relevant studies: Short-term toxicity to fish.waiving statement

Additional information:

No experimental study is required for palladium dihydroxide based on the outcome of a full TDp assay (cfr. IUCLID Section 4 'Water solubility') and the identified acute and chronic threshold values with other water soluble palladium substances.

The lowest EC50 for acute fish toxicity was determined at >30 µg Pd/L. This is the lowest acute threshold for this endpoint identified with palladium substances, but the study suffered from methodological issues. The lowest threshold identified with reliable studies is 154 µg Pd/L (cfr Environmental Read Across Justification document in IUCLID Section 13 for more details).

7.1.1.2. Long-term toxicity to fish

No relevant information available.

7.1.2. Aquatic invertebrates

7.1.2.1. Short-term toxicity to aquatic invertebrates

No relevant information available.

**Data waiving**

Information requirement: Short-term toxicity testing on aquatic invertebrates

Reason: study scientifically not necessary / other information available

Justification: the study does not need to be conducted because the substance is highly insoluble in water, hence indicating that aquatic toxicity is unlikely to occur [study scientifically not necessary / other information available]

Discussion

The following information is taken into account for short-term toxicity to aquatic invertebrates for the derivation of PNEC:

Key Information:

No experimental study is required for palladium dihydroxide based on the outcome of a full TDp assay (cfr. IUCLID Section 4 'Water solubility') and the identified acute and chronic threshold values with other water soluble palladium substances.

The 48-hour EC50 for dihydrogen tetrachloropalladate was determined at 21.4 µg Pd L⁻¹. This is the lowest threshold identified for this endpoint with soluble Pd substances (cfr Environmental Read Across Justification document in IUCLID Section 13 for more details).

Freshwater fish

Dose descriptor: EC50

Effect concentration: 21.4 µg/L

Relevant studies: Short-term toxicity to aquatic invertebrates.waiving statement

Additional information:

No experimental study is required for palladium dihydroxide based on the outcome of a full TDp assay (cfr. IUCLID Section 4 'Water solubility') and the identified acute and chronic threshold values with other water soluble palladium substances.

Three reliable studies were identified for this endpoint. The 48-hour EC50 for dihydrogen tetrachloropalladate was determined at 21.4 µg Pd L⁻¹. This is the lowest threshold identified for this endpoint with soluble Pd substances (cfr Environmental Read Across Justification document in IUCLID Section 13 for more details).

7.1.2.2. Long-term toxicity to aquatic invertebrates

No relevant information available.

7.1.3. Algae and aquatic plants

The results are summarised in the following table:

Table 7.1. Effects on algae and aquatic plants

Method	Results	Remarks
Pseudokirchneriella subcapitata (previous names: Raphidocelis subcapitata, Selenastrum capricornutum) [green algae] (algae) freshwater toxicity to aquatic algae and cyanobacteria according to guideline OECD Guideline 201 (Alga, Growth Inhibition Test) [before 23 March 2006]	EC50 (72h): 4.03 µg/L test mat. - Diamminedichloropalladium (meas. (geom. mean)) based on: yield (95% CL 3.58 - 4.85) EC50 (72h): 5.88 µg/L test mat. - Diamminedichloropalladium (meas. (geom. mean)) based on: growth rate (95% CL 5.27 - 6.22) EC50 (72h): 2.03 µg/L element - Palladium (meas. (geom. mean)) based on: yield (95% CL 1.80 - 2.44)	1 (reliable without restriction) supporting study experimental study Test material 14323-43-4 / 238-269-3, Form: solid: particulate/powder - migrated



	<p>EC50 (72h): 2.96 µg/L element - Palladium (meas. (geom. mean)) based on: growth rate (95% CL 2.65 - 3.13) NOEC (72h): 2.64 µg/L test mat. - Diamminedichloropalladium (meas. (geom. mean)) based on: yield NOEC (72h): 2.64 µg/L test mat. - Diamminedichloropalladium (meas. (geom. mean)) based on: growth rate NOEC (72h): 1.33 µg/L element - Palladium (meas. (geom. mean)) based on: yield NOEC (72h): 1.33 µg/L element - Palladium (meas. (geom. mean)) based on: growth rate EC10 (72h): 2.84 µg/L test mat. - Diamminedichloropalladium (meas. (geom. mean)) based on: yield (95% CL 2.50 - 3.16) EC10 (72h): 3.74 µg/L test mat. - Diamminedichloropalladium (meas. (geom. mean)) based on: growth rate (95% CL 2.56 - 4.45) EC10 (72h): 1.43 µg/L element - Palladium (meas. (geom. mean)) based on: yield (95% CL 1.26 - 1.59) EC10 (72h): 1.88 µg/L element - Palladium (meas. (geom. mean)) based on: growth rate (95% CL 1.29 - 2.24)</p>	<p>information: powder (full information in Annex II).</p> <p>Reference Wenzel 2012</p>
<p>Pseudokirchneriella subcapitata (previous names: Raphidocelis subcapitata, Selenastrum capricornutum) [green algae] (algae) freshwater toxicity to aquatic algae and cyanobacteria according to guideline OECD Guideline 201 (Alga, Growth Inhibition Test) [before 23 March 2006]</p>	<p>EC50 (72h): 9.94 µg/L test mat. (meas. (geom. mean)) based on: growth rate (95% CL: 9.02-10.7 µg/L) EC50 (72h): 7.2 µg/L test mat. (meas. (geom. mean)) based on: yield (95% CL 6.46-11.7 µg/L) NOEC (72h): 5.67 µg/L test mat. (meas. (geom. mean)) based on: growth rate and yield EC10 (72h): 6.25 µg/L test mat. (meas. (geom. mean)) based on: growth rate (95% CL: 5.14-7.15 µg/L) EC10 (72h): 4.87 µg/L test mat. (meas. (geom. mean)) based on: yield (95%CL 3.37-5.35 µg/L)</p>	<p>1 (reliable without restriction) supporting study experimental study</p> <p>Test material Tetraamminepalladium (II) chloride, Form: not specified (full information in Annex II).</p> <p>Reference Wenzel A 2018</p>

Data waiving

Information requirement: Growth inhibition study with algae / cyanobacteria

Reason: study scientifically not necessary / other information available

Justification: The study does not need to be conducted because the substance is highly insoluble in water, hence indicating that aquatic toxicity is unlikely to occur

Discussion**Effects on algae / cyanobacteria**

The following information is taken into account for effects on algae / cyanobacteria for the derivation of PNEC:

Key Information:



No experimental study is required for this substance based on the outcome of a full TDp assay (cfr. IUCLID Section 4 'Water solubility') and the identified acute and chronic threshold values with other water soluble palladium substances.

GLP compliant studies were performed to determine the toxicity of Diamminedichloropalladium (Wenzel, 2012) and Tetraamminepalladium(2+) dichloride (Wenzel, 2018) on the growth of the unicellular freshwater green alga *Raphidocelis subcapitata* (formerly known as *Pseudokirchneriella subcapitata*) during a 72 hours assay according to the OECD guideline 201. The geometric mean EC10 and EC50 values were calculated as 2.26 and 3.57 µg Pd/L, respectively. These are the lowest acute and chronic threshold identified with palladium substances, and serve as basis for acute and chronic ERV derivation. The geometric mean ECx values of other algal species (*S. subspicatus* and *C. reinhardtii*) are 1.8 and 2-fold higher than for *P. subcapitata*, respectively (cfr Environmental Read Across Justification document in IUCLID Section 13 for more details).

Value used for CSA:

EC50 for freshwater algae: 3.57 µg/L

EC50 for marine water algae:

EC10/LC10 or NOEC for freshwater algae: 2.26 µg/L

EC10/LC10 or NOEC for marine water algae:

Relevant studies: Toxicity to aquatic algae and cyanobacteria. waiving statement

Relevant studies: TAPd dichloride Toxicity to aquatic algae and cyanobacteria. Supporting Study - Wenzel (2018)

Relevant studies: Toxicity to aquatic algae and cyanobacteria. Supporting study Wenzel 2012

Additional information:

No experimental study is required for this substance based on the outcome of a full TDp assay (cfr. IUCLID Section 4 'Water solubility') and the identified acute and chronic threshold values with other water soluble palladium substances.

GLP compliant studies were performed to determine the toxicity of Diamminedichloropalladium (Wenzel, 2012) and Tetraamminepalladium(2+) dichloride (Wenzel, 2018) on the growth of the unicellular freshwater green alga *Raphidocelis subcapitata* (formerly known as *Pseudokirchneriella subcapitata*) during a 72 hours assay according to the OECD guideline 201. The geometric mean EC10 and EC50 values were calculated as 2.26 and 3.57 µg Pd/L, respectively. The geometric mean ECx values of other algal species (*S. subspicatus* and *C. reinhardtii*) are 1.8 and 2-fold higher than for *P. subcapitata*, respectively (cfr Environmental Read Across Justification document in IUCLID Section 13 for more details).

7.1.4. Sediment organisms

No relevant information available.

7.1.5. Other aquatic organisms

No relevant information available.

7.2. Terrestrial compartment

7.2.1. Toxicity to soil macro-organisms

No relevant information available.

7.2.2. Toxicity to terrestrial plants

No relevant information available.

7.2.3. Toxicity to soil micro-organisms



No relevant information available.

7.2.4. Toxicity to other terrestrial organisms

No relevant information available.

7.3. Atmospheric compartment

No relevant information available.

7.4. Microbiological activity in sewage treatment systems

No relevant information available.

Data waiving

Information requirement: Effects on aquatic micro-organisms

Reason: study scientifically not necessary / other information available

Justification: the study does not need to be conducted because the substance is highly insoluble in water, hence indicating that aquatic toxicity is unlikely to occur [study scientifically not necessary / other information available]

Discussion

The following information is taken into account for effects on aquatic micro-organisms for the derivation of PNEC:

Key Information:

No experimental study is required for palladium dihydroxide based on the outcome of a full TDp assay (cfr. IUCLID Section 4 'Water solubility') and the identified acute and chronic threshold values with water soluble palladium substances.

The inhibition of the total respiration of activated sludge when exposed to tetraaminepalladium hydrogen carbonate was assessed. Based on nominal concentrations, the 3-h EC50 and EC10 values were 12.56 and 5.26 mg Pd/L. These were the lowest threshold values for this endpoint (cfr Environmental Read Across Justification document in IUCLID Section 13 for more details).

Value used for CSA:

EC50/LC50 for aquatic micro-organisms: 12.56mg/L EC10/LC10 or NOEC for aquatic micro-organisms: 5.26mg/L

Relevant studies: Toxicity to microorganisms.waiving statement

7.5. Non compartment specific effects relevant for the food chain (secondary poisoning)

7.5.1. Toxicity to birds

No relevant information available.

7.5.2. Toxicity to mammals

No relevant information available.



7.6. PNEC derivation and other hazard conclusions

7.6.1. PNEC derivation and other hazard conclusions

Table 7.2. Hazard assessment conclusion for the environment

Compartment	Hazard conclusion	Remarks/Justification
Freshwater	no hazard identified: Intermittent releases:	conclusion based on TDp testing results (cfr. IUCLID Section 4 'Water solubility') and identified ERV values (cfr. 'conclusion on classification').
Marine water	no hazard identified: Intermittent releases:	conclusion based on TDp testing results (cfr. IUCLID Section 4 'Water solubility') and identified ERV values (cfr. 'conclusion on classification').
Sediments (freshwater)	no hazard identified:	conclusion based on TDp testing results (cfr. IUCLID Section 4 'Water solubility') and identified ERV values (cfr. 'conclusion on classification').
Sediments (marine water)	no hazard identified:	conclusion based on TDp testing results (cfr. IUCLID Section 4 'Water solubility') and identified ERV values (cfr. 'conclusion on classification').
Sewage treatment plant	no hazard identified:	conclusion based on TDp testing results (cfr. IUCLID Section 4 'Water solubility') and identified ERV values (cfr. 'conclusion on classification').
Soil	no hazard identified:	conclusion based on TDp testing results (cfr. IUCLID Section 4 'Water solubility') and identified ERV values (cfr. 'conclusion on classification').
Air	no hazard identified:	This substance is not expected to contribute to ozone depletion, ozone formation, global warming or acidification. Therefore, the evaluation of atmospheric risk is not required.
Secondary poisoning	no potential for bioaccumulation:	A secondary poisoning assessment is not required for this substance as it does not have the potential to cause toxic effects if accumulated in higher organisms, as it is not classified as H360 "May damage fertility or the unborn child", H361 "Suspected of damaging fertility or the unborn child", H362 "May cause harm to breastfed children", H372 "Causes damage to organs through prolonged or repeated exposure" or H373 "May cause damage to organs through prolonged or repeated exposure".

Conclusion on environmental classification

Environmental classification for the poorly water soluble Pd substances under consideration is based on the lowest acute and chronic threshold values from the Pd ecotoxicity test data combined with TDp test data generated as outlined in OECD Guidance Document on Transformation/Dissolution of Metals and Metal Compounds in Aqueous Media (OECD, 2001).

The acute and chronic ERV values have been derived as specified in the read-across justification document attached in IUCLID Section 13:

-acute ERV: lowest acute threshold value is 3.57 µg Pd/L (geometric mean EC50 value (growth rate) with P.



subcapitata, based on the experimental results for diamminedichloropalladium (EC50=2.96 μ Pd/L; Wenzel 2012) and tetraamminepalladium dichloride (EC50 = 4.31 μ g Pd/L; Wenzel 2018))
 -chronic ERV: lowest chronic threshold value is 2.26 μ g Pd/L (geometric mean EC10 value (growth rate) with P. subcapitata, based on the experimental results for diamminedichloropalladium (EC10 = 1.88 μ g Pd/L; Wenzel 2012) and tetraamminepalladium dichloride (EC10=2.72 μ g Pd/L; Wenzel 2018)).

The derivation of both ERV values is detailed in the Read-across justification report and PNEC derivation report (cfr. IUCLID Section 13).

For classification purposes, these ERVs have been recalculated to the values expressed as the concentration of the substance (conversion based on molecular weight conversion from soluble ion to the substance considered – cfr. details in below table), and compared to the TDp test results (cfr table below) as outlined in ECHA Guidance on the application of the CLP criteria (version 5.0; ECHA, 2017). Details of the TDp test results are included in IUCLID Section 4 ‘Water solubility’. Based on the results of the 24h TDp screening test (loading = 100 mg/L) at pH 6 and 8.5, full 7-d TDp (1-10-100 mg/L loading) and 28-d TDp (1 mg/L loading) assays at the worst case pH value have been performed. The metal release data are compared to the substance specific ERV values as outlined in ECHA Guidance on the application of the CLP criteria (version 5.0; ECHA, 2017) - cfr. below table. Based on the ERVs and the TDp test data, it is concluded that the metal release at all doses and durations are well below the ERV values, and that none of the substances considered need classification.

		MWt	Pd Wt%	Acute ERV (μ g TI/L)	Chronic ERV (μ g TI/L)	24h Screening*		7d TDp			28d TDp	Acute aquatic hazard	Long term aquatic hazard
						100 mg/L@pH6	100 mg/L@pH8.5	1 mg/L	10 mg/L	100 mg/L	1 mg/L		
Palladium	Pd	106.42	100.0	3.57	2.26	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	not classified	not classified
palladium monoxide	PdO	122.42	86.9	4.11	2.60	0.06	1.06	<0.05	<0.05	<0.05	<0.05	not classified	not classified
palladium dihydroxide	Pd(OH) ₂	140.44	75.8	4.71	2.98	0.1	<0.01	0.01	0.21	0.4	0.13	not classified	not classified

* values in bold give the highest metal release. The consequent 7 and 28 day tests are performed at this pH value. For Pd metal, the general observation for metals that metal release is higher at lower pH values is followed, and the 7 and 28-day tests are performed at pH 6.



8. PBT AND vPvB ASSESSMENT

8.1. Assessment of PBT/vPvB Properties

8.1.1. PBT/vPvB criteria and justification

No relevant information available.

8.1.2. Summary and overall conclusions on PBT or vPvB properties

Overall conclusion: PBT assessment does not apply.

Justification:

A PBT assessment is not required for this substance as it is inorganic.

8.2. Emission characterisation



9. EXPOSURE ASSESSMENT (and related risk characterisation)

The sections 9 and 10 of this CSR have been generated with Chesar 3.5.

9.0. Introduction

9.0.1. Overview on uses

See the description of the various uses in section 2 of the CSR.

9.0.2. Assessment entity groups

Not applicable

9.0.3. Introduction to the assessment for the environment

9.0.3.1. Tonnage

Not required since no environmental exposure assessment is needed (see scope under 9.0.3).

9.0.3.2. Scope and type of assessment for the environment

Exposure assessment and risk characterisation are not required for the environment as no hazard has been identified for the environment.

9.0.3.3. Fate and distribution parameters

Physicochemical properties used for exposure estimation

The following substance properties are used in the fate estimation done by EUSES. They correspond to the “value used for CSA” reported in sections 1 and 4.

Table 9.2. Substance key phys-chem and fate properties

Substance property	Value
Molecular weight	≥ 140.4
Molecular weight used for the assessment	140.4
Melting point at 101 325 Pa	450 °C
Water solubility	0.13 µg/L at 22.1 °C
Log K _p (solids-water in soil)	2.64 at 25 °C
Log K _p (solids-water in suspended matter)	3.39 at 23 °C

Fate (release percentage) in the modelled biological sewage treatment plant

In a standard (modelled) biological STP, the emissions are distributed in the following way:

Release to water	26.6%
Release to air	0%
Release to sludge	73.4%
Release degraded	0%

The fractions reported in the above table have been set by the assessor .

Explanation:

Stutt E, Wilson I, Merrington G & Rothenbacher K (2016) Determining the Removal of Platinum Group Metals in Industrial Effluent during Sewage Treatment.

9.0.3.4. Comments on assessment approach for the environment

The regional concentrations are reported in section 10.2.1.1. The local Predicted Exposure Concentrations (PECs) reported for each contributing scenario correspond to the sum of the local concentrations (C_{local}) and the regional concentrations (PEC regional).



9.0.3.5. Scope and type of assessment for man via environment

The exposure assessment for man via environment is not needed.

An assessment of indirect exposure of humans via the environment is generally only conducted if:

- the tonnage >1 000 t/y or
- the tonnage >100 t/Y and the substance is classified as STOT RE 1; or as a carcinogen or mutagen (any category); or as toxic to reproduction (categories 1A or 1B). (Guidance on information requirements and chemical safety assessment. Chapter R16: Environmental exposure estimation (Version 3.0, February 2016))

9.0.4. Introduction to the assessment for workers

9.0.4.1. Scope and type of assessment for workers

The scope of exposure assessment and type of risk characterisation required for workers are described in the following table based on the hazard conclusions presented in section 5.11.

Table 9.3. Type of risk characterisation required for workers

Route	Type of effect	Risk characterisation type	Hazard conclusion (see section 5.11)
Inhalation	Systemic effects - long term	Not needed	No hazard identified
	Systemic effects - acute	Not needed	No hazard identified
	Local effects - long term	Not needed	No hazard identified
	Local effects - acute	Not needed	No hazard identified
Dermal	Systemic effects - long term	Not needed	No hazard identified
	Systemic effects - acute	Not needed	No hazard identified
	Local effects - long term	Not needed	No hazard identified
	Local effects - acute	Not needed	No hazard identified
Eye	Local effects	Qualitative	Medium hazard (no threshold derived)

9.0.4.2. Comments on assessment approach for workers

Assessment approach related to toxicological hazard:

GENERAL GOOD OCCUPATIONAL HYGIENE PRACTICES

In the palladium industry, good occupational hygiene practices are followed to ensure safe handling of palladium substances. Generally, inhalation (e.g. dust should not be blown off with compressed air) and ingestion (e.g. no eating and smoking in the workplace, regular cleaning with suitable cleaning devices) are avoided. More specific measures include: (i) contaminated clothing is not taken home, (ii) good general ventilation in the workplace is always ensured, (iii) regular training in workplace hygiene practice and proper use of personal protective equipment (where relevant).

General information on risk management related to toxicological hazard:

GENERAL INFORMATION RELATED TO PERSONAL PROTECTIVE EQUIPMENT FOR WORKERS

Use of personal protective equipment for each of the exposure routes listed below is required as described here, unless exposure to the substance can be excluded for the respective route(s) of exposure. Such exclusion of exposure may be determined by: (i) the physical appearance of the substance in the specific type of application (e.g. wetting the substance can effectively prevent from the emission of dust), (ii) the emission potential resulting from the nature of the process (e.g. splashes, emission of dust can be excluded in a closed process), (iii) applied exposure prevention measures (segregation of the emission source or separation of the worker from the emission source), and (iv) the amount of the handled/emitted material during use in relation to the room size (i.e. dilution factor) under consideration of the prevailing air exchange rates during use.



EYE/FACE PROTECTION

Eye/face protective equipment is to be selected in consideration of mechanical, cold or heat stress or any other physico-chemical hazards as relevant for the conducted tasks and working environment in addition to the effectiveness of the equipment to control exposure.

9.0.5. Introduction to the assessment for consumers

Exposure assessment is not applicable as there are no consumer-related uses for the substance.



9.1. Exposure scenario 1: Manufacture - Manufacture of the substance (as such)

Environment contributing scenario(s):		
CS 1	Manufacture of the substance (as such and in mixture)	ERC 1
Worker contributing scenario(s):		
CS 2	Batch reaction in closed system	PROC 3
CS 3	Handling of solutions/Wet chemistry in open or semi-closed processes	PROC 4
CS 4	Mixing, blending	PROC 5
CS 5	Handling/Transfer of solutions	PROC 8b
CS 6	Small scale handling/Transfer of solutions	PROC 9
CS 7	Laboratory analyses	PROC 15
CS 8	Mechanical operations in open or semi-closed processes	PROC 24
CS 9	Wet cleaning	PROC 8a

Further description of the use:

Palladium dihydroxide mixtures are prepared by rising the pH of a formulation containing water soluble Palladium (II) salts solution in the presence of various metal oxide materials.

Explanation on the approach taken for the ES:

It is noted that this exposure scenario focusses on exposure to the substance to be registered. Please refer to information on safe use for the handling of the individual raw materials for process steps preceding the chemical transformation step.

9.1.1. Env CS 1: Manufacture of the substance (as such and in mixture) (ERC 1)

Exposure assessment and risk characterisation are not required (see scope under 9.0.3).

9.1.2. Worker CS 2: Batch reaction in closed system (PROC 3)

9.1.2.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
<ul style="list-style-type: none"> • Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.1.2.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.1.3. Worker CS 3: Handling of solutions/Wet chemistry in open or semi-closed processes (PROC 4)

Task(s) covered with this contributing scenario: Transfer processes, sampling, reaction.

9.1.3.1. Conditions of use



	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.1.3.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.1.4. Worker CS 4: Mixing, blending (PROC 5)

9.1.4.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.1.4.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.1.5. Worker CS 5: Handling/Transfer of solutions (PROC 8b)

9.1.5.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.1.5.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.1.6. Worker CS 6: Small scale handling/Transfer of solutions (PROC 9)

9.1.6.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	



9.1.6.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.1.7. Worker CS 7: Laboratory analyses (PROC 15)

9.1.7.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.1.7.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.1.8. Worker CS 8: Mechanical operations in open or semi-closed processes (PROC 24)

9.1.8.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.1.8.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.1.9. Worker CS 9: Wet cleaning (PROC 8a)

9.1.9.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.1.9.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation



Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.



9.2. Exposure scenario 2: Use at industrial sites - Use as an intermediate

Market sector: Manufacture of other substances

Sector of use: SU 9: Manufacture of fine chemicals

Environment contributing scenario(s):		
CS 1	Use as an intermediate	ERC 6a
Worker contributing scenario(s):		
CS 2	Handling/Transfer of solutions	PROC 8b
CS 3	Small scale handling/transfer of solutions	PROC 9
CS 4	Batch reaction process in closed system	PROC 3
CS 5	Open or semi-closed wet chemical reaction process	PROC 4
CS 6	Mixing, blending	PROC 5
CS 7	Laboratory analyses	PROC 15
CS 8	Manual handling of wetted materials	PROC 26
CS 9	Process steps at elevated temperature	PROC 22
CS 10	Wet cleaning	PROC 8a

Explanation on the approach taken for the ES:

It is noted that this exposure scenario focusses on exposure to the substance to be registered. Please refer to information on safe use for the handling of the individual manufactured substances for process steps commencing the chemical transformation step.

9.2.1. Env CS 1: Use as an intermediate (ERC 6a)

Exposure assessment and risk characterisation are not required (see scope under 9.0.3).

9.2.2. Worker CS 2: Handling/Transfer of solutions (PROC 8b)

9.2.2.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.2.2.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.2.3. Worker CS 3: Small scale handling/transfer of solutions (PROC 9)

9.2.3.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	



9.2.3.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.2.4. Worker CS 4: Batch reaction process in closed system (PROC 3)

9.2.4.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.2.4.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.2.5. Worker CS 5: Open or semi-closed wet chemical reaction process (PROC 4)

9.2.5.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.2.5.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.2.6. Worker CS 6: Mixing, blending (PROC 5)

9.2.6.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.2.6.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation



Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.2.7. Worker CS 7: Laboratory analyses (PROC 15)

9.2.7.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.2.7.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.2.8. Worker CS 8: Manual handling of wetted materials (PROC 26)

9.2.8.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.2.8.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.2.9. Worker CS 9: Process steps at elevated temperature (PROC 22)

9.2.9.1. Conditions of use

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.2.9.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.

9.2.10. Worker CS 10: Wet cleaning (PROC 8a)

9.2.10.1. Conditions of use



	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Use of eye protection: Yes <i>Use suitable eye protection.</i>	

9.2.10.2. Exposure and risks for workers

No exposure datasets are defined for this worker contributing scenario.

Risk characterisation

Qualitative risk characterisation (Eye, local):

The risk to the eyes is controlled if suitable eye protection is used.



10. RISK CHARACTERISATION RELATED TO COMBINED EXPOSURE

10.1. Human health

10.1.1. Workers

Combined exposure not relevant, no systemic effects present (see scope under 9.0.4).

10.1.2. Consumer

Exposure assessment is not applicable as there are no consumer-related uses for the substance.

10.2. Environment (combined for all emission sources)

Exposure assessment and risk characterisation are not required for the environment (see scope under 9.0.3).



Annexes



1. Annex: References

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Wenzel 2012: Effect of Diamminedichloropalladium (II) on the Growth of Pseudokirchneriella subcapitata (study report), Testing laboratory: Fraunhofer Institute for Molecular Biology and Applied Ecology (IME), 57377 Schmallenberg, Germany, Report no: WCA-001/4-30/A. Owner company; Precious Metals and Rhenium Consortium, c/o European Precious Metals Federation, Avenue de Broqueville 12, B-1150 Brussels, Belgium, Study number: Not reported, Report date: Apr 17, 2012

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2. Annex: Information on Test Material

Test material: **Palladium (II)**

Form: **gas under pressure: refrigerated liquefied gas**

Composition type: Constituent	Reference substance: Palladium (II) EC no.: CAS no.: IUPAC name: Palladium (II)	Concentration range:
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Details on test material: Plasma emission standard, in 1 M HCl Source: BDH

Test material: **Palladium (II)**

Form: **gas under pressure: refrigerated liquefied gas**

Composition type: Constituent	Reference substance: Palladium (II) EC no.: CAS no.: IUPAC name: Palladium (II)	Concentration range:
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Details on test material: Pd(NO₃)₂ in 2-3 % HNO₃, ICP standard 1000 ppm solutions (CertiPur, Merck)

Test material: **Palladium (II)**

Form: **gas under pressure: refrigerated liquefied gas**

Composition type: Constituent	Reference substance: Palladium (II) EC no.: CAS no.: IUPAC name: Palladium (II)	Concentration range:
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Details on test material: 10000 ppm Pd(II) plasma emission standard in 1.2 M HCl Source: BDH

Test material: **palladium monoxide / 1314-08-5 / 215-218-3**

Form: **not specified**

Composition type: Constituent	Reference substance: Palladium monoxide EC no.: CAS no: 1314-08-5 IUPAC name: palladium monoxide	Concentration range:
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Details on test material: - Name of test material (as cited in study report): PdO - Substance type: No data - Physical state: No data - Analytical purity: No data - Impurities (identity and concentrations): No data - Composition of test material, percentage of components: No data - Isomers composition: No data - Purity test date: No data - Lot/batch No.: No data - Expiration date of the lot/batch: No data - Stability under test conditions: No data - Storage condition of test material: No data

Test material: **palladium(2+) dihydroxide / 12135-22-7 / 235-219-2**

Form:

Composition type: Constituent	Reference substance: palladium dihydroxide EC no.: CAS no: 12135-22-7 IUPAC name: palladium(2+) dihydroxide	Concentration range:
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Details on test material: Brown solid, purity 65.3% (as Palladium), stored at room temperature in the dark

Test material: **palladium monoxide / 1314-08-5 / 215-218-3**

Form:

Composition type: Constituent	Reference substance: Palladium monoxide EC no.: CAS no: 1314-08-5 IUPAC name: palladium monoxide	Concentration range:
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Details on test material: - Name of test material (as cited in study report): Palladium monoxide - Other: no



further details given

Test material: **palladium(2+) dichloride / 7647-10-1 / 231-596-2**

Form: **not specified**

Composition type: Constituent	Reference substance: Palladium dichloride EC no.: CAS no: 7647-10-1 IUPAC name:	Concentration range:

Details on test material: - Name of test material (as cited in study report): Palladium (II) chloride - Substance type: No data - Physical state: No data - Analytical purity: No data - Impurities (identity and concentrations): No data - Composition of test material, percentage of components: No data - Isomers composition: No data - Purity test date: No data - Lot/batch No.: No data - Expiration date of the lot/batch: No data - Stability under test conditions: No data - Storage condition of test material: No data

Test material: **palladium(2+) dihydroxide / 12135-22-7 / 235-219-2**

Form: **solid: particulate/powder - migrated information: powder**

Composition type: Constituent	Reference substance: palladium dihydroxide EC no.: CAS no: 12135-22-7 IUPAC name: palladium(2+) dihydroxide	Concentration range:

Test material: **palladium(2+) dihydroxide / 12135-22-7 / 235-219-2**

Form: **solid: particulate/powder - migrated information: powder**

Composition type:	Reference substance: palladium dihydroxide EC no.: CAS no: 12135-22-7 IUPAC name: palladium(2+) dihydroxide	Concentration range:

Details on test material: - Name of test material (as cited in study report): Palladium dihydroxide - Physical state: Brown powder - Analytical purity: Pd content 71.9% w/w, which represents 94.9% w/w Pd(OH)₂ - Impurities (identity and concentrations): - Composition of test material, percentage of components: - Isomers composition: no data - Purity test date: no data - Lot/batch No.: 9045/00-F3 - Expiration date of the lot/batch: 14 June 2015 - Stability under test conditions: acceptable stability for 14 days at room temperature - Storage condition of test material: Controlled room temperature (15-25 deg C below 70 RH%)

Test material: **palladium(2+) dihydroxide / 12135-22-7 / 235-219-2**

Form: **not specified**

Composition type: Constituent	Reference substance: palladium dihydroxide EC no.: CAS no: 12135-22-7 IUPAC name: palladium(2+) dihydroxide	Concentration range:

Details on test material: - Name of test material (as cited in study report): Palladium dihydroxide - Analytical purity: 65.3 % w/w Pd - Purity test date: 28.03.2012 - Lot/batch No.: MM10121 - Other: Particle size distribution and specific surface area (BET analysis) values were taken from: Fraunhofer IKTS report N° 4198_4208_4214_4216 of 12.11.2012. - d₅₀ = 0.673 µm (50th percentile of the particle size cumulative distribution as measured by volume) - d₉₀ = 12.117 µm (90th percentile of the particle size cumulative distribution as measured by volume) - BET = 133 m²/g

Test material: **palladium(2+) dihydroxide / 12135-22-7 / 235-219-2**

Form: **not specified**

Composition type: Constituent	Reference substance: palladium dihydroxide	Concentration range:



	EC no.: CAS no: 12135-22-7 IUPAC name: palladium(2+) dihydroxide	
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Details on test material: - Name of test material (as cited in study report): Palladium dihydroxide - Analytical purity: 65.3 % w/w - Purity test date: 28/03/2012 - Lot/batch No.: MM10121 - Other: Particle size distribution and specific surface area (BET analysis) values were taken from: Fraunhofer IKTS report N° 4198_4208_4214_4216 of 12.11.2012. - $d_{50} = 0.673 \mu\text{m}$ (50th percentile of the particle size cumulative distribution as measured by volume) - $d_{90} = 12.117 \mu\text{m}$ (90th percentile of the particle size cumulative distribution as measured by volume) - BET = 133 m²/g

Test material: **14323-43-4 / 238-269-3**

Form: **solid: particulate/powder - migrated information: powder**

Composition type: Constituent	Reference substance: Diamminedichloropalladium EC no.: CAS no: 14323-43-4 IUPAC name: Diamminedichloropalladium	Concentration range:

Details on test material: - Name of test material (as cited in study report): Diamminedichloropalladium (II) - Molecular formula (if other than submission substance): Cl₂H₆N₂Pd - Molecular weight (if other than submission substance): 211.39 g/mole - Physical state: yellow powder - Analytical purity: >99.5% - Composition of test material, percentage of components: 50.33% Palladium - Lot/batch No.: 11011 - Expiration date of the lot/batch: 31 October 2012 - Storage condition of test material: Room temperature (15 - 30°C)

Test material: **Tetraamminepalladium (II) chloride**

Form: **not specified**

Composition type: Constituent	Reference substance: Tetraamminepalladium (II) chloride EC no.: CAS no: IUPAC name: Tetraamminepalladium (II) chloride	Concentration range:



3. Annex: Mode of action / Human relevance Framework

Section 5.6.3: Repeated dose toxicity_Pd dihydroxide

Detailed information on mode of action / Human relevance framework:

Section 5.7.3: Genetic toxicity

Detailed information on mode of action / Human relevance framework:

no genotoxic / mutagenic potential identified

Section 5.9.3: Toxicity to reproduction

Detailed information on mode of action / Human relevance framework: