CHEMICAL SAFETY REPORT

Substance Name: Tetraamminepalladium(2+) diacetate
EC Number: 262-819-1
CAS Number: 61495-96-3
Registrant's Identity: Predefined Legal entity

Table of Contents

List of Tables

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: CSR (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: CSR (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: CSR (all uses)

Part B

1. IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

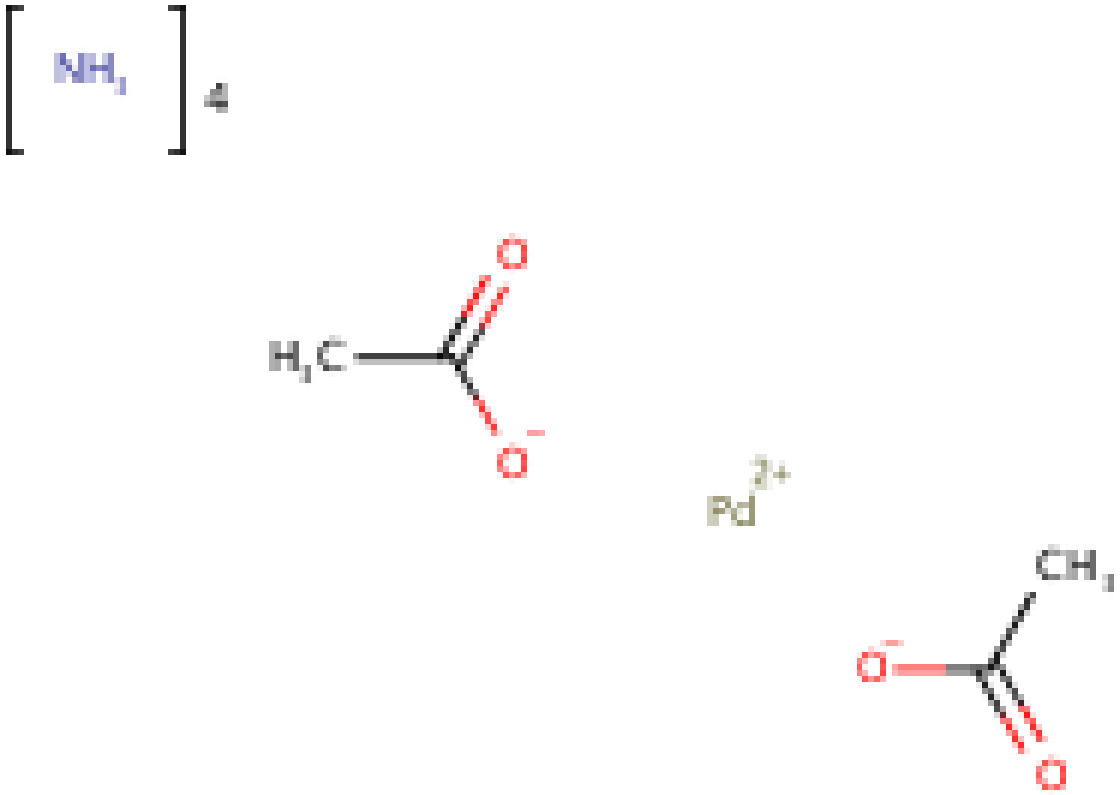
1.1. Name and other identifiers of the substance

The substance Tetraamminepalladium(2+) diacetate is a mono-constituent substance (inorganic) having the following characteristics and physical–chemical properties (see the IUCLID dataset for further details).
The following public name is used:

Table 1.1. Substance identity

EC number:	262-819-1
EC name:	tetraamminepalladium(2+) diacetate
CAS number (EC inventory):	61495-96-3
CAS number:	61495-96-3
IUPAC name:	Tetraamminepalladium(2+) diacetate
Molecular formula:	C2H3O2.1/2H12N4Pd
Molecular weight range:	292.63

Structural formula:



1.2. Composition of the substance

Overall information on composition:

Composition	Related composition(s)	Related assessment entity
Tetraamminepalladium(2+) diacetate (legal entity composition of the substance)		tetraamminepalladium(2+) diacetate
Tetraamminepalladium(2+) diacetate (boundary composition of the substance)		tetraamminepalladium(2+) diacetate Pd dissolved

Name: Tetraamminepalladium(2+) diacetate

(legal entity composition of the substance)
State/form: solid and powder
Degree of purity: % (w/w)
Description: Mono-constituent substance

Table 1.2. Constituents (Tetraamminepalladium(2+) diacetate)

Constituent	Typical concentration	Concentration range	Remarks
Tetraamminepalladium(2+) diacetate EC no.: 262-819-1	% (w/w)	% (w/w)	

Table 1.3. Impurities (Tetraamminepalladium(2+) diacetate)

Constituent	Typical concentration	Concentration range	Remarks
Chloride EC no.:	% (w/w)	% (w/w)	
water EC no.: 231-791-2	% (w/w)	% (w/w)	
ammonium acetate EC no.: 211-162-9	% (w/w)	% (w/w)	
Several minor impurities EC no.:	% (w/w)	% (w/w)	Several minor (especially metallic, e.g. Ag, Au, Cu, Ir, Pb, Pt, Rh, Ru) impurities which do not affect the classification of the substance because of their non-hazardous nature or because they do not exceed the classification cut-off limits in the substance.

Name: Tetraamminepalladium(2+) diacetate

(boundary composition of the substance)
State/form: solid and powder
Degree of purity: >=82 - <=100 % (w/w)
Description: Mono-constituent substance

Table 1.4. Constituents (Tetraamminepalladium(2+) diacetate)

Constituent	Typical concentration	Concentration range	Remarks
Tetraamminepalladium(2+) diacetate EC no.: 262-819-1	91 % (w/w)	>=82 - <=100 % (w/w)	The concentration range provided for tetraamminepalladium(2+) diacetate corresponds to a concentration between 30 and 36.4% of palladium.

Table 1.5. Impurities (Tetraamminepalladium(2+) diacetate)

Constituent	Typical concentration	Concentration range	Remarks
Chloride EC no.:	<0.1 % (w/w)	>=0 - <=0.5 % (w/w)	
water EC no.: 231-791-2	<5 % (w/w)	>=0 - <=10 % (w/w)	
ammonium acetate EC no.: 211-162-9	<5 % (w/w)	>=0 - <=8 % (w/w)	
Several minor impurities EC no.:	<0.5 % (w/w)	>=0 - <=0.5 % (w/w)	Several minor (especially metallic, e.g. Ag, Au, Cu, Ir, Pb, Pt, Rh, Ru) impurities which do not

			affect the classification of the substance because of their non-hazardous nature or because they do not exceed the classification cut-off limits in the substance.

1.3. Assessment entity information

Assessment entity name	Remarks
tetraamminepalladium(2+) diacetate	Assessment entity composition: The composition(s) for this assessment entity is the one listed in section 1.2 (Composition of the Substance)
Pd dissolved	Assessment entity composition: Palladium EC no.: Additional information: **For this category of 15 palladium substances (i.e. palladium metal and 14 inorganic palladium substances), it is proposed that, in environmental media, the substances (partly) dissolve. Only the dissolved species are capable of exerting effects on organisms. The counterions dissociate from the palladium moiety / palladium complex with the formation of [Pd(OH)2]0as the dominant Pd species and a free Pd2+-ion concentration that is vanishingly low (<<10-10M). It should be noted that this represents a chemical transformation and not a "biotransformation". The counterions do not contribute significantly to the observed effect(s), and these effects (expressed as dissolved palladium concentration) are similar for the different category members.** **More details are provided in the Read Across Justification Document, attached in IUCLID Section 13.**

1.4. Physicochemical properties

Table 1.6. Physicochemical properties

Property	Value used for CSA / Discussion	Description of key information	Assessment entity linked
Physical state	**solid at 20°C and 101.3 kPa** The appearance and physical state of tetraamminepalladium diacetate is taken from the test material section of a GLP-compliant report on the physico-chemical properties of the test material (Winkler 2016). This is considered to be suitable for use as the key study for this endpoint. Tetraamminepalladium diacetate is a light yellow solid.	Tetraamminepalladium diacetate is a light yellow solid.	

Melting / freezing point	The melting point of tetraaminepalladium (II) acetate was assessed in a GLP compliant study following OECD guideline 102 and EC method A.1 (Winkler 2016). The melting point / melting range were assessed by differential scanning calorimetry (DSC). This is a GLP-compliant, guideline study and is considered suitable for use as the key study for this endpoint. The test item decomposed before melting occurred and therefore no melting point could be determined.	The test item decomposed before melting occurred and therefore no melting point could be determined.	Pd dissolved
Boiling point	The boiling point of tetraaminepalladium (II) acetate was assessed in a GLP compliant study following OECD guideline 103 and EC method A.2 (Winkler 2016). The boiling point / boiling range were assessed by differential scanning calorimetry (DSC). This is a GLP-compliant, guideline study and is considered suitable for use as the key study for this endpoint. The test item decomposed before boiling occurred and therefore no boiling point could be determined.	The test item had no boiling point at atmospheric conditions as decomposition started before boiling occurred.	
Relative density	**1.69 at 20°C** The relative density of the test item tetraamminepalladium (II) acetate was determined in a GLP study according to OECD 109 guideline and EC method A.3 (Winkler 2016). The relative density of tetraaminepalladium (II) acetate at temperature of 20.0°C was determined to be 1.69.	The relative density of tetraamminepalladium (II) acetate at 20.0°C is 1.69.	
Granulometry	The particle size distribution of the test item was determined by the	The median particle size d(0.5) of tetraamminepalladium (II) acetate	

	particle sizing instrument Mastersizer 2000 (Michael-Schulz 2016). This is a non-GLP, non-guideline but well documented study and therefore is considered suitable for use as the key study for this endpoint. A median particle size d(0.5) of 113.185 µm was determined for a sample of tetraamminepalladium (II) acetate.	was determined to be 113.185 µm.	
Vapour pressure	**0.002Pa at 25°C** Vapour pressure is not a relevant endpoint for inorganic substances. However, as this substance has an organic component a predicted vapour pressure value for palladium diacetate is included in order to provide information on this component. Vapour pressure for palladium diacetate has been predicted using the USEPA's MPBPWIN model (USEPA 2010). The vapour pressure for palladium diacetate is very low, and is consistent with measured data that is available for ruthenium acetate (2.6 x 10-3 Pa at 25°C, Safepharm 1997). The predicted vapour pressure for palladium diacetate, representative of the organic component of tetraamminepalladium(2+) diacetate, is 0.00239 Pa at 25°C.	The predicted vapour pressure for palladium diacetate, representative of the organic component of tetraamminepalladium(2+) diacetate, is 0.00239 Pa at 25°C.	Pd dissolved
Partition coefficient n-octanol/water (log value)	**Log Kow (Log Pow): -0.17 at 20°C** The handbook "Exploring QSAR hydrophobic, electronic, and steric constants" (Hansch et al 1995) is a reliable, peer reviewed handbook and so can be considered suitable for use as the key study for this endpoint. The log kow of acetic acid, representative of the organic component of tetraamminepalladium(2+) diacetate, is -0.17.	The log kow of acetic acid, representative of the organic component of tetraamminepalladium(2+) diacetate, is -0.17.	
Water solubility	**1008g/L at 20°C** The water solubility of the test item Tetraamminepalladium(II)acetate was determined in a GLP study	The water solubility of tetraamminepalladium (2+) diacetate is >1008 g/L at 20°C.	Pd dissolved

	according to OECD 105 and EC A.6 guidelines (Winkler 2016). The water solubility of Tetraamminepalladium(II)acetate at a temperature of 20°C was determined to be >1008 g/L.		
Autoflammability / self-ignition temperature	Tetraamminepalladium (II) acetate was assessed for auto-flammability following the UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria fifth Edition (2009) and Regulation (EC) No 1272/2008 (CLP-/GHS-regulation) (Michael-Schulz 2016). Differential Scanning Calorimetry was performed to characterise the test item. During the DSC analysis Tetraamminepalladium (II) acetate showed endothermic peaks, for example melting peaks. The test item has low melting point (<160°C) and therefore does not fulfil the criteria of Class 4.2 “Self-heating Substances” of the UN-TDG and the Hazard Class “Self-heating substances and mixtures” of the Regulation (EC) No. 1272/2008 (CLP-/GHS-Regulation) as the melting process is endothermic and the substance-air surface is reduced. The full N.4 test was therefore not conducted.	Tetraamminepalladium (II) acetate does not fulfil the criteria of Class 4.2 “Self-heating Substances” of the UN-TDG and the Hazard Class “Self-heating substances and mixtures” of the Regulation (EC) No. 1272/2008 (CLP-/GHS-Regulation).	
Flammability	**not classified** The flammability of Tetraamminepalladium (II) acetate was determined in a study according the UN-Test N.1 (Michael-Schulz 2016). This is a non-GLP, guideline study and is considered suitable for use as the key study for this endpoint.	Tetraamminepalladium (II) acetate does not fulfil the criteria of Class 4.1 ‘Flammable Solids’ of the TGD and the Hazard Class ‘Flammable Solids’ of the Regulation (EC) No 1272/2008 (CLP) and GHS as the test item could not be ignited with the gas burner (burning time 2 min) in the preliminary screening test.	

Data waiving

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: Self-ignition temperature

Reason: study scientifically not necessary / other information available

Justification: the study does not need to be conducted because the substance is a solid having a melting point <= 160°C [study scientifically not necessary / other information available]

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]

Information requirement: Oxidising properties

Reason: other justification

Justification: In accordance with column 2 of REACH Annex VII, the oxidising properties study does not need to be conducted as the substance is incapable of reacting exothermically with combustible materials on the basis of its chemical structure.

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.

On the basis of the available physico-chemical data this substance is not classified for physico-chemical endpoints.

2. MANUFACTURE AND USES

2.1. Manufacture

Table 2.1. Manufacture

	Manufacture
M-1	**Manufacture of the substance (as such)** Further description of manufacturing process: Tetraammine palladium (2+) diacetate is manufactured by adding an inorganic Pd precursor to an ammine ligand and an acetate source. Contributing activity/technique for the environment : **- Manufacture of the substance (as such) ES 1.1 (ERC1)** **- Manufacture of the substance (as such) ES 1.2 (ERC1)** **- Manufacture of the substance (as such) ES 1.3 (ERC1)** Contributing activity/technique for the workers : **- Fully contained processes (PROC 1)** **- Handling/Transfer of solutions (PROC 8b)** **- Wet cleaning (PROC 8a)** use registered according to REACH Article 10; total tonnage manufactured/imported >=10tonnes/year per registrant Tonnage of substance for that use: tonnes/year Related assessment: use assessed in a joint CSR

2.2. Identified uses

No information available on identified uses.

Table 2.2. Uses at industrial sites

	Uses at industrial sites
IW-1	**Use as an intermediate** Further description of the use: Contributing activity/technique for the environment : **- Use as an intermediate ES 2.1 (ERC6a)** **- Use as an intermediate ES 2.2 (ERC6a)** **- Use as an intermediate ES 2.3 (ERC6a)** Contributing activity/technique for the workers : **- Handling/Transfer of solutions (PROC 8b)** **- Small scale handling/transfer of solutions (PROC 9)** **- Fully contained reaction process (PROC 1)** **- Closed batch reaction process (PROC 3)** **- Open or semi-closed wet chemical reaction process (PROC 4)** **- Laboratory analyses (PROC 15)** **- Wet cleaning (PROC 8a)** **Sector of end use:** SU 8: Manufacture of bulk, large scale chemicals (including petroleum products) ; SU 9: Manufacture of fine chemicals **Technical function of the substance:** intermediate (precursor) use registered according to REACH Article 10; total tonnage manufactured/imported >=10tonnes/year per registrant Tonnage of substance for that use: tonnes/year Substance supplied to that use: as such ; in a mixture

	Subsequent service life relevant for that use: no Related assessment: use assessed in a joint CSR

3. CLASSIFICATION AND LABELLING

3.1. Classification and labelling according to CLP / GHS

Substance: Tetraamminepalladium (2+) diacetate
Implementation: EU
Related composition: Boundary composition
The substance is classified as follows:

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
Flammable aerosols:			data conclusive but not sufficient for classification
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:			data conclusive but not sufficient for classification
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:	Acute Tox. 4	H302: Harmful if swallowed.	
Acute toxicity - dermal:			data conclusive but not sufficient for classification
Acute toxicity - inhalation:			data lacking
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:	Skin Sens. 1A	H317: May cause an allergic skin reaction.	
Aspiration hazard:			data lacking
Reproductive Toxicity:			data conclusive but not sufficient for classification
Reproductive Toxicity: Effects on or via lactation:			data lacking
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):	Aquatic Acute 1	H400: Very toxic to aquatic life.	
Hazards to the aquatic environment (chronic/long-term):	Aquatic Chronic 1	H410: Very toxic to aquatic life with long lasting effects.	
M-Factor acute: 10			
M-Factor chronic: 10			
Hazardous to the ozone layer:			data conclusive but not sufficient for classification

Labelling

Signal word: Warning

Hazard pictogram:

GHS07: exclamation mark

GHS09: environment

Hazard statements:

H302: Harmful if swallowed.

H317: May cause an allergic skin reaction.

H319: Causes serious eye irritation.

H400: Very toxic to aquatic life.

H410: Very toxic to aquatic life with long lasting effects.

Precautionary statements:

P101: If medical advice is needed, have product container or label at hand.

P102: Keep out of reach of children.

P103: Read carefully and follow all instructions.

P261: Avoid breathing dust/fume/gas/mist/vapours/spray.

P264: Wash ... thoroughly after handling.

P270: Do not eat, drink or smoke when using this product.

P272: Contaminated work clothing should not be allowed out of the workplace.

P273: Avoid release to the environment.

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

P301+P312: IF SWALLOWED: Call a POISON CENTER/doctor/... if you feel unwell.

P302+P352: IF ON SKIN: Wash with plenty of water/…

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

P321: Specific treatment (see ... on this label).

P330: Rinse mouth.

P333+P313: If skin irritation or rash occurs: Get medical advice/attention.

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

P362+P364: Take off contaminated clothing and wash it before reuse.

P391: Collect spillage.

P501: Dispose of contents/container to ...

4. ENVIRONMENTAL FATE PROPERTIES

General discussion of environmental fate and pathways:

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. This method is used for organic substances to measure the decomposition or degradation of a chemical reacting with water and for inorganics this type of method is not appropriate. This substance is an organo-metallic substance, but the organic component of the substance is readily biodegradable and assessment of hydrolysis is not required for readily biodegradable substances. As this substance consists of inorganic and readily biodegradable organic components, hydrolysis is not considered to be relevant.

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.

4.2. 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	2 (reliable with restrictions) supporting study experimental study **Test material** Palladium (II), Form: gas under

	phase: Transformation products:	pressure: refrigerated 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:

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. For the exposure assessment the log Kd value from the suspended solids was used in case no value was available.

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

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

Assessment entity linked:
Pd dissolved. View the assessment entity table in chapter 1.3 **here**

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.

4.3. 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:

With its relatively low molecular weight (~330 g/mol) and, more critically, high water solubility (100 g/L), it is likely that tetraamminepalladium diacetate will be absorbed (as the ions) from the gastro intestinal tract. As such, predicted oral absorption of tetraamminepalladium diacetate is conservatively set at 100%.

Although not expected to reach the lungs in appreciable quantities (since the substance is marketed as a solution with a low predicted vapour pressure [for the organic component of the substance]), as a highly water soluble substance with a relatively low molecular weight, any tetraamminepalladium diacetate reaching the lungs is likely to be absorbed through aqueous pores. As such, the predicted inhalation absorption is conservatively set at 100%.
Tetraamminepalladium diacetate, with water solubility in excess of 10,000 mg/L, may be unable to cross the lipid-rich environment of the stratum corneum, especially considering the low dermal penetration expected for metals as well as the low partition coefficient of -0.17 [for the organic component of the substance]. Moreover, tetraamminepalladium diacetate lacks skin irritation potential (which could, in theory, disrupt skin barrier function). As such, predicted dermal absorption is conservatively set at 10%.

Once absorbed, distribution and excretion are expected to be rapid, with little or no bioaccumulation occurring, due to its highly water soluble nature. 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). Based on expert ECHA guidance, the relatively low molecular weight (~330 g/mol) and, more critically, the high estimated water solubility (100 g/L) are indicative of a high bioavailability of tetraamminepalladium diacetate by this route. Moreover, the partition coefficient (log Pow) of acetic acid, representative of the organic component of tetraamminepalladium diacetate, is -0.17 (Hansch, 1995) which is favourable (between -1 and 4) for absorption by passive diffusion. A health-precautionary assumption is that the ions will be absorbed from the gastro-intestinal tract. As such, predicted oral absorption of tetraamminepalladium diacetate is set at 100%.

In an acute oral study on the structurally related tetraamminepalladium hydrogen carbonate, necropsy revealed changes in the lungs, liver, kidneys and small intestine (Allen, 1995a), indicating a degree of oral absorption. In a 28-day gavage toxicity study on the same “tetraamminepalladium salts” category member (source substance), various of the toxic effects, which included reductions in body weight, growth, food consumption and kidney weight, as well as changes in blood parameters (in males) and histological effects in the spleen, liver and kidneys (Wragg, 1997), were indicative of absorption. Slower growth in rats in a repeated-dose reproduction toxicity study on tetraamminepalladium dichloride, a different source substance (Grosz, 2015) also indicated absorption. Overall, absorption is expected for ingested tetraamminepalladium diacetate.

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). Palladium diacetate has the same organic component as tetraamminepalladium diacetate, and has a very low QSAR-predicted vapour pressure (0.00239 Pa at 25°C; USEPA, 2010), indicating that only a small proportion of the latter substance may be available for inhalation as a vapour. Particle size distribution testing was waived as the substance is marketed in a “non-solid or granular form” (as a solution). Accordingly, inhalation is not considered to be a significant route of exposure. However, as a highly water soluble substance (>10,000 mg/L), any tetraamminepalladium diacetate reaching the lungs is likely to be absorbed through aqueous pores or be retained in the mucus and transported out of the respiratory tract by absorption. Overall, while it is very unlikely that tetraamminepalladium diacetate will be available to a high extent via the lungs, it is considered health precautionary 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. Given the high water solubility of tetraamminepalladium diacetate (100 g/L), it is unlikely to be able to cross the lipid-rich environment of the stratum corneum. Moreover, dermal penetration is likely to be limited by the poor lipophilicity of the organic portion of the molecule, as represented by acetic acid (log Pow <0). 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). However, 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, tetraamminepalladium diacetate is not classified for skin irritation. This is based on the lack of irritation potential observed in rabbits with the structurally related compounds tetraamminepalladium dichloride and tetraamminepalladium hydrogen carbonate (Allen, 1995b; Driscoll, 1981). Given the low penetration expected from metals, the high water solubility (and, thus, low expected lipophilicity), and the lack of skin irritation potential (which could, in theory, disrupt skin barrier function and facilitate dermal penetration), 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 tetraamminepalladium diacetate.

No overt toxicity was seen in rats in an acute dermal study on the structurally related compound tetraamminepalladium hydrogen carbonate (Allen, 1997a). Effects were similarly absent in in vivo skin irritation (Allen, 1995b; Driscoll, 1981) and skin sensitisation (Allen, 1997b, 2000) studies on the source substances tetraamminepalladium dichloride and tetraamminepalladium hydrogen carbonate (though these are limited in their assessment of systemic effects). Overall, there is limited evidence to suggest that the substance will not be well-absorbed dermally.

Distribution/Metabolism

Once absorbed, distribution of tetraamminepalladium and acetate ions throughout the body is expected based on a relatively low molecular weight.

Rats given the structurally related compound tetraamminepalladium hydrogen carbonate showed alterations in the lungs, liver, kidneys and small intestine) (Allen, 1995a), which might suggest distribution to these sites. In a 28-day gavage toxicity study on the category member, tetraamminepalladium hydrogen carbonate, there were histological effects in the spleen, liver and kidneys of rats (Wragg, 1997), possibly indicative of distribution to these tissues.

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 having a molecular weight above 300 g/mol (molecular weights below this figure are considered to be associated with favourable excretion in the rat (ECHA, 2014)), rapid excretion is likely based on high water solubility of the substance and ions. 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, tetraamminepalladium diacetate is considered to have only a low potential for bioaccumulation based on its predicted physico-chemical properties (i.e. water solubility >10,000 mg/L).

Conclusion

Based on the physico-chemical properties, the chemical structure, molecular weight and the results of toxicity studies, as well as limited toxicokinetic data on other palladium compounds, tetraamminepalladium diacetate is likely partially bioavailable by the oral route and rapidly excreted once absorbed. A high dermal bioavailability is unlikely, particularly as the substance is anticipated to be highly water soluble and poorly lipophilic with a lack of skin irritation potential. Although bioavailability by the inhalation route is anticipated to be low (since the substance is marketed as a solution and has low predicted vapour pressure), inhalation absorption is considered a possibility based on its low molecular weight and high water solubility. 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
rat [common species] (Sprague-Dawley [rat]) male/female oral: unspecified according to OECD Guideline 401 (Acute Oral Toxicity) [before 2002] ; according to EU Method B.1 (Acute Toxicity (Oral))	LD50: 933 mg/kg bw (female) based on: (test mat.)	2 (reliable with restrictions) key study experimental study **Test material** 134620-00-1 / 134620-00-1; Tetraammine palladium hydrogen carbonate, Form: not specified (full information in **Annex II**). **Reference** **Allen DJ 1995**
rat [common species] (Sprague-Dawley [rat]) male/female oral: unspecified according to OECD Guideline 401 (Acute Oral Toxicity) [before 2002] ; according to EU Method B.1 (Acute Toxicity (Oral))	LD50: 933 mg/kg bw (female) based on: (test mat.)	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**). **Reference** **Allen DJ 1995**
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable to each of the category member substances.		

5.2.1.2. Acute toxicity: inhalation

No relevant information available.

Data waiving

Information requirement: Acute toxicity after inhalation exposure

Reason: other justification

Justification: 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. As the substance is marketed or used in a non solid or granular form, inhalation will not be a significant route of exposure. Palladium diacetate has the same organic component as tetraamminepalladium diacetate, and has a very low QSAR predicted vapour pressure (0.00239 Pa at 25°C; USEPA, 2010), indicating that only a small proportion of the latter substance may be available for inhalation as a vapour. Further, tetraamminepalladium diacetate is classified as a skin sensitiser. Given that skin sensitisation may be acquired by other routes of exposure than dermal, appropriate risk management measures/operational controls (RMMs/OCs) are required. These will ensure that the potential for inhalation exposure is minimised. Finally, for animal welfare reasons, conducting new in vivo toxicity tests is considered a last resort. Consequently, no testing by the inhalation route is considered justified.

5.2.1.3. Acute toxicity: dermal

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

Table 5.2. Studies on acute toxicity after dermal administration

Method	Results	Remarks
rat [common species] (Sprague-Dawley [rat]) male/female Coverage: semiocclusive Vehicle: unchanged (no vehicle) according to OECD Guideline 402 (Acute Dermal Toxicity) [before 9 Oct. 2017] ; according to EU Method B.3 (Acute Toxicity (Dermal))	LD50: >2000 mg/kg bw (male) based on: (test mat.) (CL not applicable) LD50: >2000 mg/kg bw (female) based on: (test mat.) (CL not applicable)	2 (reliable with restrictions) key study experimental study **Test material** 134620-00-1 / 134620-00-1; Tetramminepalladium (II) hydrogen carbonate, Form: solid (full information in **Annex II**). **Reference** **Allen DJ 1997**
rat [common species] (Sprague-Dawley [rat]) male/female Coverage: semiocclusive Vehicle: unchanged (no vehicle) according to OECD Guideline 402 (Acute Dermal Toxicity) [before 9 Oct. 2017] ; according to EU Method B.3 (Acute Toxicity (Dermal))	LD50: >2000 mg/kg bw (male) based on: (test mat.) (CL not applicable) LD50: >2000 mg/kg bw (female) based on: (test mat.) (CL not applicable)	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**). **Reference** **Allen DJ 1997**
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on		

three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable to each of the category member substances.

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:

In an OECD guideline study, the acute oral LD50 of tetraamminepalladium hydrogen carbonate in female rats was reported to be 933 mg/kg bw (Allen, 1995a).

In an OECD guideline study, to GLP, the acute dermal LD50 of tetraamminepalladium hydrogen carbonate was found to be greater than 2000 mg/kg bw, as no deaths occurred at this limit dose (Allen, 1997a).

No relevant acute inhalation toxicity data were identified.

Value used for CSA:
Acute oral toxicity:
adverse effect observed
(LD50) 933mg/kg bw
Acute dermal toxicity:
no adverse effect observed
Acute inhalation toxicity:
no study available

Additional information:

No relevant acute toxicity human data were identified.

The acute oral toxicity of tetraamminepalladium hydrogen carbonate was assessed in rats, in a study conducted according to OECD Test Guideline 401. In the range finding study, one male and one female rat received a single dose of 2000 mg/kg bw by oral gavage. The male was found dead two days after dosing whereas the female had no signs of systemic toxicity at day 5. Therefore, in the main study, groups of 5 females were administered 500, 1000 or 2000 mg/kg bw of the test material and a group of 5 male rats received 2000 mg/kg bw. All 10 rats receiving 2000 mg/kg bw died by day 3 of the observation period, whilst 3 of 5 females receiving 1000 mg/kg bw died on days 4 to 6. No deaths were seen in the low dose females, following the 14-day observation period. The study authors conclude that the acute oral median lethal dose (LD50) of the test

material in female rats is 933 mg/kg bw. “No significant difference in toxicity was noted between male and female animals” (Allen, 1995a).

The acute dermal toxicity of tetraamminepalladium hydrogen carbonate was evaluated in an OECD Test Guideline 402 study, conducted according to GLP. The test material was applied to the shaved skin of rats (5/sex), under a semi-occlusive covering, and removed (by gentle washing) after 24 hr. There were no signs of systemic toxicity or mortality during the 14-day observation period, and no adverse pathology was found. Therefore, the acute dermal LD50 of the test material was found to be greater than 2000 mg/kg bw (Allen, 1997a).

Tetraamminepalladium hydrogen carbonate is considered to fall within the scope of the read-across category “tetraamminepalladium salts”. See IUCLID section 13 for full read-across justification report.

No acute inhalation toxicity data were identified. However, 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 selection of acute toxicity – oral endpoint
OECD guideline study, with limitations, and the only acute oral toxicity study available.

Justification for selection of acute toxicity – dermal endpoint
GLP, OECD guideline study, and the only acute dermal toxicity study available.

Justification for classification or non classification:

Based on the results of the available and reliable acute oral rat study with tetraamminepalladium hydrogen carbonate, tetraamminepalladium dichloride should be classified for acute oral toxicity (category 4) according to EU CLP criteria (EC 1272/2008).

No classification for acute dermal toxicity is required, based on the results of the available and reliable acute dermal rat study with tetraamminepalladium hydrogen carbonate.

No clear evidence of specific target organ toxicity was noted. As such, classification for STOT-SE is not considered appropriate.

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 5.3. Studies on skin irritation

Method	Results	Remarks

rabbit [common species] (New Zealand White [rabbit]) Coverage: occlusive (shaved) Vehicle: water according to OECD Guideline 404 (Acute Dermal Irritation / Corrosion)	GHS criteria not met primary dermal irritation index (PDII) 0 of max. 8 (Time point: Mean of 1, 24, 48 and 72 hr time points) Reversibility: no irritation observed erythema score 0 of max. 8 (Time point: Mean of 1, 24, 48 and 72 hr time points) Reversibility: no irritation observed edema score 0 of max. 8 (Time point: Mean of 1, 24, 48 and 72 hr time points) Reversibility: no irritation observed	2 (reliable with restrictions) key study experimental study **Test material** 13815-17-3 / 237-489-7; Tetraamminepalladium dichloride, (full information in **Annex II**). **Reference** **Driscoll SR 1981**
rabbit [common species] (New Zealand White [rabbit]) Coverage: occlusive (shaved) Vehicle: water according to OECD Guideline 404 (Acute Dermal Irritation / Corrosion)	GHS criteria not met primary dermal irritation index (PDII) 0 of max. 8 (Time point: Mean of 1, 24, 48 and 72 hr time points) Reversibility: no irritation observed erythema score 0 of max. 8 (Time point: Mean of 1, 24, 48 and 72 hr time points) Reversibility: no irritation observed edema score 0 of max. 8 (Time point: Mean of 1, 24, 48 and 72 hr time points) Reversibility: no irritation observed	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**). **Reference** **Driscoll SR 1981**
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable to each of the category member substances.		
rabbit [common species] (New Zealand White [rabbit]) Coverage: semiocclusive (intact) Vehicle: not specified according to OECD Guideline 404 (Acute Dermal Irritation / Corrosion) ; according to EU Method B.4 (Acute Toxicity: Dermal Irritation / Corrosion)	GHS criteria not met primary dermal irritation index (PDII) 0 (Time point: 1, 24, 48 and 72-hour observations) Reversibility: not applicable	2 (reliable with restrictions) key study experimental study **Test material** 134620-00-1 / 134620-00-1; Tetraamminepalladium hydrogen

		carbonate, Form: not specified (full information in **Annex II**). **Reference** **Allen DJ 1995**
rabbit [common species] (New Zealand White [rabbit]) Coverage: semiocclusive (intact) Vehicle: not specified according to OECD Guideline 404 (Acute Dermal Irritation / Corrosion) ; according to EU Method B.4 (Acute Toxicity: Dermal Irritation / Corrosion)	GHS criteria not met primary dermal irritation index (PDII) 0 (Time point: 1, 24, 48 and 72-hour observations) Reversibility: not applicable	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**). **Reference** **Allen DJ 1995**
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable to each of the category member substances.		

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

Data waiving

Information requirement: Skin Irritation

Reason: study scientifically not necessary / other information available

Justification: an in vitro skin irritation study does not need to be conducted because adequate data from an in vivo skin irritation study are available [study scientifically not necessary / other information available]

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 5.4. Studies on eye irritation

Method	Results	Remarks
in vitro study Chicken. (Cobb 500) Vehicle: unchanged (no vehicle) - The test item was supplied as a solution and applied without further dilution. according to EU method B.48 (Isolated chicken eye test method for identifying occular corrosives and severe irritants) ; according to OECD Guideline 438 (Isolated Chicken Eye Test Method for Identifying Ocular Corrosives and Severe Irritants) [before 26 July 2013]	GHS criteria not met cornea opacity score Maximal mean corneal opacity score at 240 mins. Maximum score of 4.0; value 0.33 fluorescein retention score Fluorescein retention (mean) at 30 mins. Maximum score of 3.0; value 1 percent corneal swelling Maximal corneal swelling (mean) at 240 mins. Maximum score of 100; value 1.6	1 (reliable without restriction) key study experimental study **Test material** 61495-96-3 / 262-819-1; Tetramminepalladium diacetate, Form: aqueous solution (full information in **Annex II**). **Reference** **Hargitai J 2014**
rabbit (New Zealand White [rabbit]) Vehicle: unchanged (no vehicle) according to OECD Guideline 405 (Acute Eye Irritation / Corrosion)	Category 2 (irritating to eyes) based on GHS criteria maximum mean total score (MMTS) (mean) 27 (Time point: 1, 24, 48 and 72 hr, and 7 days) not fully reversible within: 7 days in two of the three animals maximum mean total score (MMTS) - with rinsing (mean) 31 (Time point: 1, 24, 48 and 72 hr, and 7 days) not fully reversible within: 7 days in two of the rabbits	2 (reliable with restrictions) key study experimental study **Test material** 13815-17-3 / 237-489-7; Tetraamminepalladium (II) dichloride, Form: solid: particulate/powder - migrated information: powder (full information in **Annex II**). **Reference** **Driscoll SR and Collier TA 1981**
rabbit (New Zealand White [rabbit]) Vehicle: unchanged (no vehicle) according to OECD Guideline 405 (Acute Eye Irritation / Corrosion)	Category 2 (irritating to eyes) based on GHS criteria maximum mean total score (MMTS) (mean) 27 (Time point: 1, 24, 48 and 72 hr, and 7 days) not fully reversible within: 7 days in two of the three animals maximum mean total score (MMTS) - with rinsing (mean) 31 (Time point: 1, 24, 48 and 72 hr, and 7 days) not fully reversible within: 7 days in two of the rabbits	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**).

		Reference **Driscoll SR and Collier TA 1981**
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable to each of the category member substances.		
rabbit (New Zealand White [rabbit]) Vehicle: unchanged (no vehicle) according to OECD Guideline 405 (Acute Eye Irritation / Corrosion) ; according to EU Method B.5 (Acute Toxicity: Eye Irritation / Corrosion)	Category 1 (irreversible effects on the eye) based on GHS criteria overall irritation score (animal: single animal tested) 53 of max. 110 (Time point: 1 hour) animal killed at 24 hr for humane reasons overall irritation score (animal: single animal tested) 81 of max. 110 (Time point: 24 hours) animal killed at 24 hr for humane reasons cornea opacity score (animal: single animal tested) 40 of max. 80 (Time point: 1 hour) animal killed at 24 hr for humane reasons cornea opacity score (animal: single animal tested) 60 of max. 80 (Time point: 24 hours) animal killed at 24 hr for humane reasons iris score (animal: single animal tested) 5 of max. 10 (Time point: 1 hour) animal killed at 24 hr for humane reasons iris score (animal: single animal tested) 5 of max. 10 (Time point: 24 hours) animal killed at 24 hr for humane reasons conjunctivae score (animal: single animal tested) 8 of max. 20 (Time point: 1 hour) animal killed at 24 hr for humane	2 (reliable with restrictions) key study experimental study **Test material** 134620-00-1 / 134620-00-1; Tetramminepalladium hydrogen carbonate, Form: solid: particulate/powder - migrated information: powder (full information in **Annex II**). **Reference** **Allen DJ 1995**

	reasons conjunctivae score (animal: single animal tested) 16 of max. 20 (Time point: 24 hours) animal killed at 24 hr for humane reasons	
rabbit (New Zealand White [rabbit]) Vehicle: unchanged (no vehicle) according to OECD Guideline 405 (Acute Eye Irritation / Corrosion) ; according to EU Method B.5 (Acute Toxicity: Eye Irritation / Corrosion)	Category 1 (irreversible effects on the eye) based on GHS criteria overall irritation score (animal: single animal tested) 53 of max. 110 (Time point: 1 hour) animal killed at 24 hr for humane reasons overall irritation score (animal: single animal tested) 81 of max. 110 (Time point: 24 hours) animal killed at 24 hr for humane reasons cornea opacity score (animal: single animal tested) 40 of max. 80 (Time point: 1 hour) animal killed at 24 hr for humane reasons cornea opacity score (animal: single animal tested) 60 of max. 80 (Time point: 24 hours) animal killed at 24 hr for humane reasons iris score (animal: single animal tested) 5 of max. 10 (Time point: 1 hour) animal killed at 24 hr for humane reasons iris score (animal: single animal tested) 5 of max. 10 (Time point: 24 hours) animal killed at 24 hr for humane reasons conjunctivae score (animal: single animal tested) 8 of max. 20 (Time point: 1 hour) animal killed at 24 hr for humane reasons conjunctivae score (animal: single animal tested) 16 of max. 20 (Time point: 24 hours)	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**). **Reference** **Allen DJ 1995**

	animal killed at 24 hr for humane reasons	
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable to each of the category member substances.		

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:

In two in vivo OECD guideline skin irritation studies, no irritant or corrosive reactions were observed following 4-hr application of tetraamminepalladium dichloride (under occlusion) or tetraamminepalladium hydrogen carbonate (semi-occlusion) to the intact shaved skin of three New Zealand white rabbits in each case (Allen, 1995b; Driscoll, 1981).

In an in vitro OECD guideline study, conducted to GLP, tetraamminepalladium diacetate was found to be non-irritating to isolated chicken eyes (Hargitai, 2014). However, in two previously conducted OECD guideline eye irritation studies with New Zealand white rabbits, moderate to severe irritation was seen following instillation of undiluted tetraamminepalladium dichloride (Driscoll and Collier, 1981) or tetraamminepalladium hydrogen carbonate (Allen, 1995c).

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

Additional information:

No relevant irritation/corrosion human data were identified. No in vitro skin or eye irritation studies were identified, or are required, as reliable in vivo studies are already available.

In an OECD Test Guideline 404 study, neat tetraamminepalladium dichloride (0.5 g, moistened) was applied (occluded) to the clipped but intact skin of three New Zealand white rabbits. After 4 hours, the dressings were removed and the skin sites assessed for signs of irritation (oedema and erythema/eschar) and corrosion at 1, 24, 48 and 72 hours. No irritation (erythema/eschar formation or erythema) or corrosion of the skin was seen at any time point during the 72-hr study period. The primary irrational index was therefore 0, and tetraamminepalladium dichloride was classified as non-irritating (Driscoll, 1981).

In another study conducted to OECD Test Guideline 404, a 4-hr semi-occluded application of an unspecified amount of tetraamminepalladium hydrogen carbonate was made to the intact skin [details on preparation of test site not known] of 2 female and 1 male New Zealand white rabbit. Yellow-staining was noted at all treated skin sites at 1, 24, 48 and 72 hrs. No erythema/eschar or oedema were seen at any of the four observation points. The test material produced a primary irritation index of 0 and was considered as non-irritant to rabbit skin according to the Draize classification system. No corrosive effects were noted (Allen, 1995b).

In an in vitro OECD Test Guideline 438 study, conducted according to GLP, tetraamminepalladium diacetate was assessed for potential irritating effects in isolated chicken eyes. One of the eyes was treated with physiological saline (negative control), three eyes with the test item (30 µL) and another three eyes with 5% w/v benzalkonium chloride (positive control). After 10 seconds, the surface of the eyes was rinsed with physiological saline. Corneal thickness, corneal opacity and fluorescein retention were measured and any morphological effects (e.g. pitting or loosening of the epithelium) evaluated. No evidence of treatment-related corrosion or severe irritation to the isolated chicken eyes was observed. The positive and negative controls gave the expected results, confirming the validity of the test (Hargitai, 2014).

However, eye irritation was observed in two previously conducted in vivo studies on two closely-related surrogates.

In an OECD Test Guideline 405 study, to GLP, undiluted tetraamminepalladium dichloride (100 mg, powdered) was instilled into the right eye of each of six New Zealand white rabbits. The contralateral eye remained untreated and was used for control purposes. In half of the animals, the eyes were rinsed after 30 seconds with 100 ml of sterile distilled water. Moderate to severe irritation was observed in the ‘non-rinsed group’, which (although reduced in severity) was not fully reversible in two of the three rabbits within 7 days after treatment. When the eyes were rinsed after a 30-second exposure, the test substance caused severe eye irritation in all three rabbits which (although reduced in severity) still persisted at day 7 in two of the animals. No clinical signs of systemic toxicity were reported. Tetraamminepalladium dichloride caused severe irritation to the eye of rabbits observed for a 7-day period (Driscoll and Collier, 1981).

In another study conducted to OECD Test Guideline 405, to GLP, tetraamminepalladium hydrogen carbonate produced a maximum group mean score of 81.0 [maximum total score possible = 110] at 24 hours and was classified as at least a very severe eye irritant to the rabbit eye according to a modified Kay and Calandra classification system. The animal was killed at 24 hours for humane reasons. Due to the severity of the effects, the test material was considered to be severely irritating to the eyes (Allen, 1995c).

Tetraamminepalladium dichloride and hydrogen carbonate are considered to fall within the scope of the read-across category “tetraamminepalladium salts”. See IUCLID section 13 for full read-across justification report.

No respiratory tract data were identified. A new study was not conducted as 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 in vivo skin irritation studies on closely-related surrogates, tetraamminepalladium dichloride does need not be classified for skin irritation according to EU CLP criteria (EC 1272/2008).

Based on the results of an in vitro eye irritation study with tetraamminepalladium diacetate, no classification is required for such effects. However, eye irritation was observed in two previously conducted in vivo studies on closely-related surrogates. As such, it seems prudent to classify tetraamminepalladium diacetate as an eye irritant (category 2), according to EU CLP criteria (EC 1272/2008).

5.4. Corrosivity

5.4.1. Non-human information

No relevant information available.

5.4.2. Human information

No relevant information available.

5.4.3. Summary and discussion of corrosion

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
guinea pig (Dunkin-Hartley [guinea pig]) male skin sensitisation: in vivo (non-LLNA) according to OECD Guideline 406 (Skin Sensitisation) ; according to EU Method B.6 (Skin Sensitisation)	Category 1A (indication of significant skin sensitising potential) based on GHS criteria No. with positive reactions: 2nd reading : 6 out of 10 (test group ; 48 h after challenge; dose: 2%) (Reading: 2nd reading. . Hours after challenge: 48.0. Group: test group. Dose level: 2%. No with. + reactions: 6.0.	2 (reliable with restrictions) key study experimental study **Test material** 13815-17-3 / 237-489-7;

	Total no. in groups: 10.0. Clinical observations: No evidence of adverse effects.) No. with positive reactions: 2nd reading : 5 out of 10 (test group ; 48 h after challenge; dose: 1%) (Reading: 2nd reading. . Hours after challenge: 48.0. Group: test group. Dose level: 1%. No with. + reactions: 5.0. Total no. in groups: 10.0. Clinical observations: No evidence of adverse effects.) No. with positive reactions: 1st reading : 0 out of 5 (negative control ; 24 h after challenge; dose: 1 and 2%) (see Remark - Reading: 1st reading. . Hours after challenge: 24.0. Group: negative control. Dose level: 1 and 2%. No with. + reactions: 0.0. Total no. in groups: 5.0. Clinical observations: One animal was found dead on day 14 from causes not related to the test material. No other clinical signs were evident..) No. with positive reactions: 2nd reading : 0 out of 5 (negative control ; 48 h after challenge; dose: 1 and 2%) (see Remark - Reading: 2nd reading. . Hours after challenge: 48.0. Group: negative control. Dose level: 1 and 2%. No with. + reactions: 0.0. Total no. in groups: 5.0. Clinical observations: One animal was found dead on day 14 from causes not related to the test material. No other clinical signs were evident..)	Tetraamminepalladium dichloride, (full information in **Annex II**). **Reference** **Allen DJ 2000**
guinea pig (Dunkin-Hartley [guinea pig]) male skin sensitisation: in vivo (non-LLNA) according to OECD Guideline 406 (Skin Sensitisation) ; according to EU Method B.6 (Skin Sensitisation)	Category 1A (indication of significant skin sensitising potential) based on GHS criteria No. with positive reactions: 2nd reading : 6 out of 10 (test group ; 48 h after challenge; dose: 2%) (Reading: 2nd reading. . Hours after challenge: 48.0. Group: test group. Dose level: 2%. No with. + reactions: 6.0. Total no. in groups: 10.0. Clinical observations: No evidence of adverse effects.) No. with positive reactions: 2nd reading : 5 out of 10 (test group ; 48 h after challenge; dose: 1%) (Reading: 2nd reading. . Hours after challenge: 48.0. Group: test group. Dose level: 1%. No with. + reactions: 5.0. Total no. in groups: 10.0. Clinical observations: No evidence of adverse effects.)	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**). **Reference** **Allen DJ 2000**

	No. with positive reactions: 1st reading : 0 out of 5 (negative control ; 24 h after challenge; dose: 1 and 2%) (see Remark - Reading: 1st reading. . Hours after challenge: 24.0. Group: negative control. Dose level: 1 and 2%. No with. + reactions: 0.0. Total no. in groups: 5.0. Clinical observations: One animal was found dead on day 14 from causes not related to the test material. No other clinical signs were evident..) No. with positive reactions: 2nd reading : 0 out of 5 (negative control ; 48 h after challenge; dose: 1 and 2%) (see Remark - Reading: 2nd reading. . Hours after challenge: 48.0. Group: negative control. Dose level: 1 and 2%. No with. + reactions: 0.0. Total no. in groups: 5.0. Clinical observations: One animal was found dead on day 14 from causes not related to the test material. No other clinical signs were evident..)	
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable to each of the category member substances.		
guinea pig (not specified) not specified skin sensitisation: in vivo (non-LLNA) according to OECD Guideline 406 (Skin Sensitisation) ; according to EU Method B.6 (Skin Sensitisation)	Category 1A (indication of significant skin sensitising potential) based on GHS criteria No. with positive reactions: 1st reading : 10 out of 10 (test group ; 24 h after challenge; dose: 1 and 2%) (see Remark - Reading: 1st reading. . Hours after challenge: 24.0. Group: test group. Dose level: 1 and 2%. No with. + reactions: 10.0. Total no. in groups: 10.0. Clinical observations: Erythema seen in all animals at challenge with 1 and 2%. Oedema seen in seven animals at 1% and all ten animals at 2% challenge..) No. with positive reactions: 1st reading : 0 out of 5 (negative control ; 24 h after challenge; dose: 1 and 2%) (Reading: 1st reading. . Hours after challenge: 24.0. Group: negative control. Dose level: 1 and 2%. No with. + reactions: 0.0. Total no. in groups: 5.0. Clinical observations: No erythema or oedema seen in any of the controls.)	2 (reliable with restrictions) key study experimental study **Test material** 134620-00-1 / 134620-00-1; Tetraamminepalladium hydrogen carbonate, (full information in **Annex II**). **Reference** **Allen DJ 1997**

	No. with positive reactions: 2nd reading : 10 out of 10 (test group ; 48 h after challenge; dose: 1 and 2%) (see Remark - Reading: 2nd reading. . Hours after challenge: 48.0. Group: test group. Dose level: 1 and 2%. No with. + reactions: 10.0. Total no. in groups: 10.0. Clinical observations: Erythema recorded in all ten animals at both concentrations. Oedema was recorded in two animals at 1% and in four animals at 2%. Desquamation was also seen in two guinea pigs..) No. with positive reactions: 2nd reading : 0 out of 5 (negative control ; 48 h after challenge; dose: 1 and 2%) (Reading: 2nd reading. . Hours after challenge: 48.0. Group: negative control. Dose level: 1 and 2%. No with. + reactions: 0.0. Total no. in groups: 5.0. Clinical observations: No erythema or oedema seen in any of the controls.)	
guinea pig (not specified) not specified skin sensitisation: in vivo (non-LLNA) according to OECD Guideline 406 (Skin Sensitisation) ; according to EU Method B.6 (Skin Sensitisation)	Category 1A (indication of significant skin sensitising potential) based on GHS criteria No. with positive reactions: 1st reading : 10 out of 10 (test group ; 24 h after challenge; dose: 1 and 2%) (see Remark - Reading: 1st reading. . Hours after challenge: 24.0. Group: test group. Dose level: 1 and 2%. No with. + reactions: 10.0. Total no. in groups: 10.0. Clinical observations: Erythema seen in all animals at challenge with 1 and 2%. Oedema seen in seven animals at 1% and all ten animals at 2% challenge..) No. with positive reactions: 1st reading : 0 out of 5 (negative control ; 24 h after challenge; dose: 1 and 2%) (Reading: 1st reading. . Hours after challenge: 24.0. Group: negative control. Dose level: 1 and 2%. No with. + reactions: 0.0. Total no. in groups: 5.0. Clinical observations: No erythema or oedema seen in any of the controls.) No. with positive reactions: 2nd reading : 10 out of 10 (test group ; 48 h after challenge; dose: 1 and 2%) (see Remark - Reading: 2nd reading. . Hours after challenge: 48.0. Group: test group. Dose level: 1 and 2%. No with. + reactions: 10.0. Total no. in groups: 10.0. Clinical observations: Erythema recorded in all ten animals at both concentrations. Oedema was	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**). **Reference** **Allen DJ 1997**

	recorded in two animals at 1% and in four animals at 2%. Desquamation was also seen in two guinea pigs..) No. with positive reactions: 2nd reading : 0 out of 5 (negative control ; 48 h after challenge; dose: 1 and 2%) (Reading: 2nd reading. . Hours after challenge: 48.0. Group: negative control. Dose level: 1 and 2%. No with. + reactions: 0.0. Total no. in groups: 5.0. Clinical observations: No erythema or oedema seen in any of the controls.)	
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable to each of the category member substances.		

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 adequate data from an in vivo skin sensitisation study are available [study scientifically not necessary / other information available]

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

In two OECD Test Guideline 406 in vivo guinea pig maximisation tests (GPMTs), to GLP, both of the structurally related compounds (tetraamminepalladium dichloride and tetraamminepalladium hydrogen

carbonate) induced skin sensitisation in at least 60% of the treated animals (Allen, 1997b, 2000).

Value used for CSA: adverse effect observed (sensitising)
Additional information:

No relevant human sensitisation data were identified. No in vitro skin sensitisation studies were identified, or are required, as reliable in vivo studies are already available.

Tetraamminepalladium dichloride was assessed for its contact sensitising potential in a guinea pig maximum test (GPMT) conducted according to OECD Test Guideline 406, and to GLP. A group of ten male animals were induced by intradermal injection of 0.1% of the test material (in distilled water), with and without Freund's Complete Adjuvant, followed 7 days later by topical exposure to 10% (in distilled water) under an occluded patch. Challenge doses of 1 and 2% (in distilled water) were applied to different sites 14 days later and the areas examined at 24 and 48 hr for erythema and oedema. A further group of five males were used as controls, receiving the same induction procedure but without the test substance, and challenged similarly to the treatment group. Six of the ten treated animals showed evidence of sensitisation at 48 hr (erythema, grade 1 or 2); three further animals exhibited erythema at 24 hr but not at 48 hr and these reactions were therefore considered not to be due to sensitisation. Tetraamminepalladium dichloride exhibited moderate skin sensitising potential in this study (Allen, 2000).

In another OECD Guideline GPMT, tetraamminepalladium hydrogen carbonate was assessed for its contact sensitising potential. The test substance was administered to ten guinea pigs (induction phase) by intradermal injection (presumably in combination with Freund's Complete Adjuvant) at a concentration of 0.01% (in arachis oil) and topically (48-hr patch test) at 5% (again in arachis oil). A challenge (presumably 10-14 days after the induction phase) to the (presumably hairless and intact) skin of ten treated guinea-pigs and five control animals was applied (24-hr patch test) at a concentration of 1 and 2% in arachis oil. The skin was observed 24- and 48-hr after patch removal for erythema, oedema and other skin reactions. Erythema was seen in all treated animals 24 and 48 hr after challenge with 1 and 2% of the test material. Oedema was seen in seven of the treated animals at 1% and in all ten treated animals at 2%, 24 hr after removal of the challenge patch tests. The number of animals with oedema was reduced to two and four, 48 hr after removal of the 1 and 2% challenge patch tests, respectively. Desquamation was also seen in two guinea pigs. All animals gained weight over the study period, and body weight gains from day 0 to day 24 appeared comparable between the treated and control groups. In summary, a GPMT involving a topical challenge application of tetraamminepalladium hydrogen carbonate at a concentration of 1 and 2% to the skin of ten guinea pigs produced sensitisation reactions in all animals; a 100% (10/10) sensitisation rate. No reactions were recorded on the skin of five control animals (Allen, 1997b).

Tetraamminepalladium dichloride and hydrogen carbonate are considered to fall within the scope of the read-across category "tetraamminepalladium salts". See IUCLID section 13 for full read-across justification report.

Justification for selection of skin sensitisation endpoint:
GLP study, conducted according to OECD guidelines.

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

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.

Justification for classification or non classification:

Based on the results of the available and reliable GPMTs on structurally-related compounds, tetraamminepalladium diacetate should be classified as a (strong) skin sensitiser (category 1A) 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 repeated dose toxicity: oral [deactivated phrase] - other: Reproduction/Developmental Toxicity Screening Test (oral: gavage) Vehicle: an aqueous ammonium-chloride buffer (NH4Cl/NH4OH) was selected as the vehicle. The vehicle allowed formulation of a stable solution of the test item, considered suitable for the study purpose. Exposure: Males were dosed for 28 days (14 days pre-mating and 14 days mating/post- mating period). They were then euthanized and subjected to necropsy examination. Females were dosed for 14 days pre-mating, for up to 7 days mating period, through gestation and up to and including the day before necropsy (at least 4 days post-partum dosing). The day of birth (viz. when parturition was complete) is defined as Day 0 post-partum. (Once daily) according to OECD Guideline 421 (Reproduction / Developmental Toxicity	NOAEL: 100 mg/kg bw/day (nominal) (female) based on: (test mat.) clinical signs ; mortality ; body weight and weight gain ; food consumption and compound intake ; organ weights and organ / body weight ratios ; gross pathology ; histopathology: non-neoplastic ; histopathology: neoplastic NOAEL: 4 mg/kg bw/day (nominal) (male) based on: (test mat.) Decreased body weight gain at 20 and 100 mg/kg bw/day.	2 (reliable with restrictions) key study experimental study **Test material** 13815-17-3 / 237-489-7; Tetraamminepalladium dichloride, Form: solid (full information in **Annex II**). **Reference** **Török-Bathó M 2015**

Screening Test)		
rat [common rodent species] (Wistar [rat]) male/female repeated dose toxicity: oral [deactivated phrase] - other: Reproduction/Developmental Toxicity Screening Test (oral: gavage) Vehicle: an aqueous ammonium-chloride buffer (NH4Cl/NH4OH) was selected as the vehicle. The vehicle allowed formulation of a stable solution of the test item, considered suitable for the study purpose. Exposure: Males were dosed for 28 days (14 days pre-mating and 14 days mating/post- mating period). They were then euthanized and subjected to necropsy examination. Females were dosed for 14 days pre-mating, for up to 7 days mating period, through gestation and up to and including the day before necropsy (at least 4 days post-partum dosing). The day of birth (viz. when parturition was complete) is defined as Day 0 post-partum. (Once daily) according to OECD Guideline 421 (Reproduction / Developmental Toxicity Screening Test)	NOAEL: 100 mg/kg bw/day (nominal) (female) based on: (test mat.) clinical signs ; mortality ; body weight and weight gain ; food consumption and compound intake ; organ weights and organ / body weight ratios ; gross pathology ; histopathology: non-neoplastic ; histopathology: neoplastic NOAEL: 4 mg/kg bw/day (nominal) (male) based on: (test mat.) Decreased body weight gain at 20 and 100 mg/kg bw/day.	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**). **Reference** **Török-Bathó M 2015**
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable to each of the category member substances.		
rat [common rodent species] (Sprague-Dawley [rat]) male/female short-term repeated dose toxicity: oral (oral: gavage) Vehicle: water Exposure: 28 days (Once daily) according to EU Method B.7 (Repeated Dose (28 Days) Toxicity (Oral))	NOAEL: 15 mg/kg bw/day (nominal) (male/female) based on: (test mat.) histopathology (treatment-related hepatic, splenic, renal and gastric abnormalities)	2 (reliable with restrictions) key study experimental study **Test material** 134620-00-1 / 134620-00-1; Tetrammine Palladium Hydrogen Carbonate, Form: solid: particulate/powder - migrated information: powder (full information in **Annex II**).

		Reference **Wragg MS, Thomas ON, Bartlett AJ, Brooks PN 1997** **Harleman JH 1997**
rat [common rodent species] (Sprague-Dawley [rat]) male/female short-term repeated dose toxicity: oral (oral: gavage) Vehicle: water Exposure: 28 days (Once daily) according to EU Method B.7 (Repeated Dose (28 Days) Toxicity (Oral))	NOAEL: 15 mg/kg bw/day (nominal) (male/female) based on: (test mat.) histopathology (treatment-related hepatic, splenic, renal and gastric abnormalities)	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material** 134620-00-1 / 134620-00-1; Tetrammine Palladium Hydrogen Carbonate, Form: solid: particulate/powder - migrated information: powder (full information in **Annex II**). **Reference** **Wragg MS, Thomas ON, Bartlett AJ, Brooks PN 1997** **Harleman JH 1997**
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable to each of the category member substances.		

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 421 reproductive/developmental toxicity screening study, to GLP, in rats with tetraamminepalladium dichloride, the general systemic toxicity NOAEL for males was the lowest tested dose (4 mg/kg bw/day), on the basis of reduced growth at 20 and 100 mg/kg bw/day (Török-Bathó, 2015). The critical oral NOAEL for tetraamminepalladium dichloride (4 mg/kg bw/day) equates to NOAELs of 1.76 and 5.45 mg/kg bw/day for palladium and tetraamminepalladium diacetate, respectively (based on MWt ratios).

In a GLP guideline study (EU Method B.7), rats were gavaged with tetraamminepalladium hydrogen carbonate for 28 days. A NOAEL of 15 mg/kg bw/day was obtained based on microscopic changes in the spleen in high-dose animals (150 mg/kg bw/day) (Wragg et al., 1997).

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):
adverse effect observed
(NOAEL: 4mg/kg bw/day; subacute, rat [common rodent species])

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. However, a reliable reproduction/developmental screening toxicity study and a 28-day oral gavage repeated dose toxicity (both in rats) have been conducted with tetraamminepalladium dichloride and tetraamminepalladium hydrogen carbonate, respectively.

Tetraamminepalladium dichloride and hydrogen carbonate are considered to fall within the scope of the read-across category “tetraamminepalladium salts”. See IUCLID section 13 for full read-across justification report.

In the first of these, in a OECD Test Guideline 421 reproductive/developmental toxicity study, conducted according to GLP, rats (12/sex/group) received a solution of tetraamminepalladium dichloride by gavage at substance doses of 0, 4, 20, or 100 mg/kg bw/day for at least 28 days (males were dosed for 28 days in total, while females received treatment for a longer period of time [incorporating the gestation period and proceeding up until postpartum day 4, i.e. around 7-8 weeks]). This reproductive and developmental screening assay has some limitations compared to a standard repeated dose assay for assessing general systemic toxicity (e.g. no haematology, clinical chemistry or urinalysis, and histopathology was limited to the high dose group). Effects on the glandular stomach (including discolouration, inflammation, and congestion) were seen in the high-dose animals, and likely reflect a local effect of treatment. These effects in the glandular stomach may have contributed to the significantly reduced body weight gain seen in males at 20 and 100 mg/kg bw/day (growth of females was unaffected). Although likely a consequence of local effects on the stomach, the no-observed-adverse-effect level (NOAEL) for systemic toxicity was 4 mg/kg bw/day on the basis of reduced growth in males at 20 and 100 mg/kg bw/day (Török-Bathó, 2015). [This NOAEL of 4 mg/kg bw/day is used as the health-precautionary critical point of departure for DNEL derivation purposes.] The critical oral NOAEL for tetraamminepalladium dichloride (4 mg/kg bw/day) equates to NOAELs of 1.76 and 5.45 mg/kg bw/day for palladium and tetraamminepalladium diacetate, respectively (based on MWt ratios).

In support, the repeated dose toxicity of tetraamminepalladium hydrogen carbonate was assessed in a 28-day oral GLP study conducted according to EU Method B.7. Groups of Sprague-Dawley rats (5/sex) were given a daily gavage administration of tetraamminepalladium hydrogen carbonate at 0 (distilled water), 1.5, 15 or 150 mg/kg bw/day for 28 days. Throughout the study, animals were observed daily for mortality and other overt clinical signs of toxicity. Body weight and food and water consumption were monitored. At the end of the study, blood samples were taken for haematological and clinical chemistry assessments, and animals were killed and subject to gross necropsy. The major organs of all animals were weighed, and the adrenals, heart, kidneys, liver, spleen, stomach and testes of high-dose and control animals were examined microscopically. Having been identified as possible target organs, the liver, spleen, kidneys and stomach were subsequently examined microscopically in all treated and control animals. No unscheduled deaths or treatment-related overt clinical signs of toxicity were seen over the course of the study. During study week 3, growth was reduced in high-dose males and females, and high-dose males demonstrated reduced food consumption and food efficiency – but these effects were not seen during week 4. High-dose males demonstrated reduced haemoglobin, erythrocyte count, haematocrit and mean corpuscular volume, with two rats having unusually high reticulocyte counts. A slight but significant rise in eosinophil levels was seen in high-dose females. At necropsy, absolute and relative kidney weights were increased in high-dose females. One high-dose male had a pale liver, kidney and glandular gastric epithelium, while one high-dose female had a reddened glandular gastric epithelium. A draft commentary on the report notes that the “degree of pigment deposition in the spleen varies marked in rats” and that the “absence of pigment deposition is indicative of a toxicologic effect”. However, “slight variations of pigment deposition are normal and do not have any physiological, pathological, or toxicological significance”. Therefore, the overall NOAEL was considered to be 15 mg/kg bw/day, with the critical effect being microscopic changes in the spleen (no haemosiderin deposition in 5/5 males and 2/5 females, compared to 0 controls) in high-dose animals. Changes seen in the stomach have been considered indicative of local irritation (Wragg et al., 1997).

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:
Reliable reproductive/developmental screening study involving repeated dosing of the parental animals for at

least 28 days and assessment for systemic toxicity, conducted to OECD guidelines and GLP, with a lower critical effect level (NOAEL) than determined in the 28-day (read-across) study.

Justification for classification or non classification:

No significant systemic effects sufficient for classification were seen in reliable guideline studies (28-day oral repeated dose and a reproductive/developmental screening assay) with tetraamminepalladium hydrogen carbonate and tetraamminepalladium dichloride, respectively. The adverse effects seen at 150 mg/kg bw/day in the repeated dose study and (reduced growth) at 20 and 100 mg/kg bw/day in the reproductive/developmental screening assay are likely the result of local toxicity in the gastrointestinal tract, and are not considered sufficient for classification as STOT-RE. As such, the results of these studies indicate that classification 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
bacterial reverse mutation assay [in vitro gene mutation study in bacteria] (in vitro gene mutation study in bacteria - Type of genotoxicity: gene mutation) S. typhimurium TA 1535, TA 1537, TA 98 and TA 100 [bacteria] (with and without met. act.) S. typhimurium TA 1538 [bacteria] (with and without met. act.) Test concentrations: 0, 50, 150, 500, 1500 and 5000 µg/plate in preliminary cytotoxicity test 0, 0.15 (Expt 1 only), 0.5, 1.5, 5, 15, 50 (-S9) 0, 1.5, 5, 15, 50, 150, 500 (Expt 1 only) (+S9) Positive control substance(s): 9-aminoacridine Positive control substance(s): 4-nitroquinoline-N-oxide Positive control substance(s): 4-nitro-o-phenyl enediamine Positive control substance(s): N-ethyl-N-nitro-N-nitrosoguanidine Positive control substance(s): 2-aminoanthracene according to OECD Guideline 471 (Bacterial Reverse Mutation Assay) [in vitro gene mutation study in bacteria] ;	Test results: negative for S. typhimurium TA 100 [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity - The test material caused a visible reduction in the growth of the bacterial lawn at 50 and 150 µg/plate and above for tester strains without and with metabolic activation respectively vehicle controls valid: valid negative controls valid: not applicable positive controls valid: valid Test results: negative for S. typhimurium TA 1535 [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity - The test material caused a visible reduction in the growth of the bacterial lawn at 50 and 150 µg/plate and above for tester strains without and with metabolic activation respectively vehicle controls valid: valid negative controls valid: not applicable positive controls valid: valid Test results: negative for S. typhimurium TA 1538	2 (reliable with restrictions) key study experimental study **Test material** 134620-00-1 / 134620-00-1; Tetramminepalladium hydrogen carbonate, Form: solid: particulate/powder - migrated information: powder (full information in **Annex II**). **Reference** **Thompson PW 1997**

according to EU Method B.13/14 (Mutagenicity - Reverse Mutation Test Using Bacteria) [in vitro gene mutation study in bacteria]	[bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity - The test material caused a visible reduction in the growth of the bacterial lawn at 50 and 150 µg/plate and above for tester strains without and with metabolic activation respectively vehicle controls valid: valid negative controls valid: not applicable positive controls valid: valid Test results: negative for S. typhimurium TA 98 [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity - The test material caused a visible reduction in the growth of the bacterial lawn at 50 and 150 µg/plate and above for tester strains without and with metabolic activation respectively vehicle controls valid: valid negative controls valid: not applicable positive controls valid: valid Test results: negative for S. typhimurium TA 1537 [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity - The test material caused a visible reduction in the growth of the bacterial lawn at 50 and 150 µg/plate and above for tester strains without and with metabolic activation respectively vehicle controls valid: valid negative controls valid: not applicable positive controls valid: valid Remarks: strain/cell type: TA 100 - Migrated from field 'Test system'.	
bacterial reverse mutation assay [in vitro gene mutation study in bacteria] (in vitro gene mutation study in bacteria - Type of genotoxicity: gene mutation) S. typhimurium TA 1535, TA 1537, TA 98 and TA 100 [bacteria] (with and without met. act.) S. typhimurium TA 1538 [bacteria] (with and without met. act.) Test concentrations: 0, 50, 150, 500, 1500 and 5000 µg/plate in preliminary cytotoxicity test 0, 0.15 (Expt 1 only), 0.5, 1.5, 5, 15, 50 (-S9) 0, 1.5, 5, 15, 50, 150, 500 (Expt 1 only) (+S9) Positive control substance(s): 9-aminoacridine Positive control substance(s): 4-	Test results: negative for S. typhimurium TA 100 [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity - The test material caused a visible reduction in the growth of the bacterial lawn at 50 and 150 µg/plate and above for tester strains without and with metabolic activation respectively vehicle controls valid: valid negative controls valid: not applicable positive controls valid: valid Test results: negative for S. typhimurium TA 1535 [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity:	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**). **Reference** **Thompson PW**

nitroquinoline-N-oxide Positive control substance(s): 4-nitro-o-phenyl enediamine Positive control substance(s): N-ethyl-N-nitro-N-nitrosoguanidine Positive control substance(s): 2-aminoanthracene according to OECD Guideline 471 (Bacterial Reverse Mutation Assay) [in vitro gene mutation study in bacteria] ; according to EU Method B.13/14 (Mutagenicity - Reverse Mutation Test Using Bacteria) [in vitro gene mutation study in bacteria]	cytotoxicity - The test material caused a visible reduction in the growth of the bacterial lawn at 50 and 150 µg/plate and above for tester strains without and with metabolic activation respectively vehicle controls valid: valid negative controls valid: not applicable positive controls valid: valid Test results: negative for S. typhimurium TA 1538 [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity - The test material caused a visible reduction in the growth of the bacterial lawn at 50 and 150 µg/plate and above for tester strains without and with metabolic activation respectively vehicle controls valid: valid negative controls valid: not applicable positive controls valid: valid Test results: negative for S. typhimurium TA 98 [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity - The test material caused a visible reduction in the growth of the bacterial lawn at 50 and 150 µg/plate and above for tester strains without and with metabolic activation respectively vehicle controls valid: valid negative controls valid: not applicable positive controls valid: valid Test results: negative for S. typhimurium TA 1537 [bacteria]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity - The test material caused a visible reduction in the growth of the bacterial lawn at 50 and 150 µg/plate and above for tester strains without and with metabolic activation respectively vehicle controls valid: valid negative controls valid: not applicable positive controls valid: valid Remarks: strain/cell type: TA 100 - Migrated from field ‘Test system’.	**1997**
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable		

to each of the category member substances.		
mammalian cell gene mutation assay [gene mutation] (in vitro gene mutation study in mammalian cells - Type of genotoxicity: gene mutation) mouse lymphoma L5178Y cells [mammalian cell line] (with and without met. act.) Test concentrations: Cytotoxicity range-finder experiment: 91.47, 182.9, 365.9, 731.8, 1464 and 2927 µg/mL (both with and without S9) Experiment 1: 75, 150, 200, 240, 270, 300, 325, 350, 375, 400 and 500 µg/mL (without S9) and 50, 100, 150, 200, 240, 270, 300, 325, 350, 375 and 450 µg/mL (with S9) Experiment 2: 25, 50, 100, 150, 200, 230, 260, 290, 320, 350 and 400 µg/mL (without S9) and 50, 100, 150, 200, 230, 260, 290, 320, 350, 380, 450 and 500 µg/mL (with S9) Positive control substance(s): 4-nitroquinoline 1-oxide (NQO; without S9) and benzo[a]pyrene (B[a]P; with S9) according to OECD Guideline 476 (In Vitro Mammalian Cell Gene Mutation Test) [in vitro gene mutation study in mammalian cells]	Test results: negative for mouse lymphoma L5178Y cells [mammalian cell line]; met. act.: with and without genotoxicity: negative cytotoxicity: cytotoxicity - Seven days after treatment, concentrations of 350-400 µg/mL (Exp 1, without S9); 450 µg/mL (Exp 1, with S9); 400 µg/mL (Exp 2, without S9) and 500 µg/mL (Exp 2, with S9) were considered too toxic for selection to determine viability and 6TG resistance. vehicle controls valid: valid negative controls valid: not applicable positive controls valid: valid Remarks: all strains/cell types tested - Migrated from field ‘Test system’.	1 (reliable without restriction) key study experimental study **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**). **Reference** **Lloyd M 2015**

Data waiving

Information requirement: In vitro genotoxicity: (in vitro cytogenicity / micronucleus study)

Reason: study scientifically not necessary / other information available

Justification: an in vitro cytogenicity study in mammalian cells or in vitro micronucleus study does not need to be conducted because adequate data from an in vivo cytogenicity test are available [study scientifically not necessary / other information available]

5.7.1.2. In vivo data

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

Table 5.8. In vivo genotoxicity studies

Method	Results	Remarks
micronucleus assay [chromosome aberration] (in vivo mammalian somatic cell study: cytogenicity / erythrocyte micronucleus - Type of genotoxicity: chromosome aberration) mouse (not specified) male oral: unspecified cyclophosphamide - Justification for choice of positive control(s): no data - Route of administration: oral - Doses / concentrations: 50 mg/kg bw	Genotoxicity: negative (male) toxicity: yes - Premature deaths were seen in the 24-hour 500 mg/kg bw (2) and 125 mg/kg bw (1) test material groups. Clinical signs were observed in animals dosed with the test material at and above 125 mg/kg bw in both the 24 and 48-hour groups, where applicable. vehicle controls valid: valid negative controls valid: not examined positive controls valid: valid Remark:	2 (reliable with restrictions) key study experimental study **Test material** 134620-00-1 / 134620-00-1; Tetraamminepalladium hydrogen carbonate, Form: not specified

according to OECD Guideline 474 (Mammalian Erythrocyte Micronucleus Test) [in vivo mammalian somatic cell study: cytogenicity / erythrocyte micronucleus] ; according to EU Method B.12 (Mutagenicity - In Vivo Mammalian Erythrocyte Micronucleus Test) [in vivo mammalian somatic cell study: cytogenicity / erythrocyte micronucleus]		(full information in **Annex II**). **Reference** **Durward R 1998**
micronucleus assay [chromosome aberration] (in vivo mammalian somatic cell study: cytogenicity / erythrocyte micronucleus - Type of genotoxicity: chromosome aberration) mouse (not specified) male oral: unspecified cyclophosphamide - Justification for choice of positive control(s): no data - Route of administration: oral - Doses / concentrations: 50 mg/kg bw according to OECD Guideline 474 (Mammalian Erythrocyte Micronucleus Test) [in vivo mammalian somatic cell study: cytogenicity / erythrocyte micronucleus] ; according to EU Method B.12 (Mutagenicity - In Vivo Mammalian Erythrocyte Micronucleus Test) [in vivo mammalian somatic cell study: cytogenicity / erythrocyte micronucleus]	Genotoxicity: negative (male) toxicity: yes - Premature deaths were seen in the 24-hour 500 mg/kg bw (2) and 125 mg/kg bw (1) test material groups. Clinical signs were observed in animals dosed with the test material at and above 125 mg/kg bw in both the 24 and 48-hour groups, where applicable. vehicle controls valid: valid negative controls valid: not examined positive controls valid: valid Remark:	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**). **Reference** **Durward R 1998**
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable to each of the category member substances.		

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 guideline study, to GLP, tetraamminepalladium hydrogen carbonate was not mutagenic in a bacterial reverse mutation (Ames) assay using five Salmonella typhimurium strains (TA98, TA100, TA1535, TA1537 and TA1538), when tested at up to cytotoxic concentrations in the presence and absence of a rat liver metabolic activation (S9) system (Thompson, 1997).

In an OECD guideline study, to GLP, tetraamminepalladium diacetate solution failed to induce mutations at the hprt locus of mouse lymphoma (L5178Y) cells when tested up to toxic concentrations in two independent experiments, each in the absence and presence of S9 (Lloyd, 2015).

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):

In an in vivo study, conducted to comply with OECD Test Guideline 474, tetraamminepalladium hydrogen carbonate failed to induce a significant increase in the frequency of micronuclei in polychromatic erythrocytes of mice following oral gavage at up to 500 mg/kg bw (Durward, 1998).

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

Justification for classification or non classification

No evidence of genotoxic activity has been seen in reliable in vitro assays in bacterial or mammalian somatic cells, including GLP guideline studies assessing mutagenic and clastogenic activity, nor in a reliable in vivo study assessing chromosome damage. No studies specifically assessing the mutagenic activity in germ cells were identified. However, no effects on reproductive parameters were seen in the reproductive/developmental toxicity screening assay. As such, classification of tetraamminepalladium diacetate for germ cell mutagenicity is not warranted, according to EU CLP criteria (EC 1272/2008).

Additional information:

No studies conducted in humans were identified (although in vitro studies using human lymphocytes are described below).

Tetraamminepalladium hydrogen carbonate was assessed for potential mutagenic activity in a bacterial reverse mutation (Ames) assay, conducted according to OECD Test Guideline 471, and to GLP. The test compound was tested in five strains of Salmonella typhimurium (TA98, TA100, TA1535, TA1537 and TA1538). (However, a strain capable of detecting certain oxidising mutagens and/or cross-linking agents, for example TA102, was not included.) The dose ranges were determined in a preliminary assay for cytotoxicity and were 0.15-50 and 1.5-500 µg/plate with and without the addition of a rat liver homogenate metabolising (S9) system. All assays were carried out in triplicate, at up to 50 and 500 µg/plate in the absence and presence of S9, respectively. The experiment was repeated. Tetraamminepalladium hydrogen carbonate showed no evidence of a dose-related increase in revertant frequency at any dose levels in any strain, either in the presence or absence of S9 (Thompson, 1997). This study lacks a bacterial strain susceptible to oxidative mutagenesis or cross-linking agents, for example TA102. However, tetraamminepalladium compounds are not expected to cause oxidative damage or to be cross-linking agents. This is based primarily on the negative Ames results in studies utilising TA102/E.coli, and negative SOS Chromotest with E.coli, conducted with related palladium compounds and also the reassuring results (mutagenicity and cytogenicity) in the available in vitro studies (including SOS Chromotest and in mammalian cells) as well as an in vivo study in mice with various tetraamminepalladium compounds (see below for details). As such this Ames study is considered sufficient for satisfying this REACH requirement and as support for the non-classification of tetraamminepalladium compounds for mutagenicity].

Tetraamminepalladium diacetate was assessed for its ability to induce mutations at the hprt locus in an in vitro mouse lymphoma assay conducted in accordance with OECD Test Guideline 476 and to GLP. Mouse lymphoma (L5178Y) cells were exposed to test material for 3 hr in two independent experiments, each in the absence and presence of S9. Concentrations of 75 to 500 µg/mL and 50 to 450 µg/mL (Experiment 1, without and with S9, respectively) and 25 to 400 µg/mL and 50 to 500 µg/mL (Experiment 2, without and with S9, respectively) were used. Cytotoxicity was observed 7 days after treatment at the highest tested levels, with concentrations of 350-400 µg/mL (Experiment 1, without S9); 450 µg/mL (Experiment 1, with S9); 400 µg/mL (Experiment 2, without S9) and 500 µg/mL (Experiment 2, with S9) being considered too toxic for selection to determine viability and 6TG resistance. Statistically significant increases in mutant frequency (MF) over the concurrent vehicle control value were observed in Experiment 2 in the presence of S9, at the highest two

concentrations analysed (380 and 450 µg/mL) but not in the absence of S9 or with or without S9 in Experiment 1. The mean MF values at 380 and 450 µg/mL were 3.84 and 2.34 mutants/10^6 viable cells, respectively, compared to the concurrent vehicle control MF value of 1.11. These increases were small in magnitude and were statistically significant because of a rather low vehicle control value (the historical control value was 3.25). Furthermore, there was no evidence of reproducibility between experiments in the presence of S9 and no statistically significant linear trends in Experiments 1 and 2, therefore the small, non-reproducible increases seen in Experiment 2 were considered not biologically relevant. Overall tetraamminepalladium diacetate solution did not induce mutation at the hprt locus of mouse lymphoma (L5178Y) cells when tested up to toxic concentrations in two independent experiments, each in the absence and presence of S9 (Lloyd, 2015).

An in vivo study was performed to assess the potential of tetraamminepalladium hydrogen carbonate to induce damage to chromosomes or aneuploidy when administered orally to mice. The study design complied with OECD Test Guideline 474 and EU Method B12. Following a range-finding study, groups of seven male mice were given 125, 250 or 500 (the MTD) mg/kg bw of the test material and killed 24 or 48 hours later for analysis of micronuclei in polychromatic and normochromatic erythrocytes. Further groups of mice were given arachis oil or cyclophosphamide as vehicle and positive controls, respectively. There was no evidence of a significant increase in the incidence of micronucleated polychromatic erythrocytes in animals dosed with the test material when compared to the concurrent vehicle control groups. No statistically significant decreases in the PCE/NCE ratio were observed in the 24- or 48-hr test material dose groups when compared to their concurrent control groups. However, premature deaths and other clinical signs indicated that systemic absorption had occurred. The positive control material produced a marked increase in the frequency of micronucleated polychromatic erythrocytes, confirming the sensitivity of the test system. In conclusion, tetraamminepalladium hydrogen carbonate failed to induce chromosome damage following oral gavage at up to 500 mg/kg bw, under the conditions of the test (Durward, 1998).

Tetraamminepalladium hydrogen carbonate is considered to fall within the scope of the read-across category “tetraamminepalladium salts”. See IUCLID section 13 for full read-across justification report.

Justification for selection of genetic toxicity endpoint
GLP study, 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.

5.9. 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 5.9. 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: 4 mg/kg bw/day Basis: other: nominal dose Doses / Concentrations: 20 mg/kg bw/day Basis: other: nominal dose Doses / Concentrations: 100 mg/kg bw/day Basis: other: nominal dose Vehicle: an aqueous ammonium-chloride buffer (NH4Cl/NH4OH) was selected as the vehicle. The vehicle allowed formulation of a stable solution of the test item, considered suitable for the study purpose. Exposure: Males were dosed for 28 days (14 days pre-mating and 14 days mating/post- mating period). They were then euthanized and subjected to necropsy examination. Females were dosed for 14 days pre-mating, for up to 7 days mating period, through gestation and up to and including the day before necropsy (at least 4 days post-partum dosing). The day of birth (viz. when parturition was complete) is defined as Day 0 post-partum. (Once daily) according to OECD Guideline 421 (Reproduction / Developmental Toxicity Screening Test)	**First parental generation (P0)** NOAEL - fertility/reproductive parameters (PO) 100 mg/kg bw/day (nominal)) (male/female) based on: reproductive function (sperm measures) [reproductive toxicity] ; reproductive performance [reproductive toxicity] NOAEL - general toxicity (PO) 100 mg/kg bw/day (nominal)) (female) based on: clinical signs [general toxicity] ; mortality [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] ; histopathology: neoplastic [general toxicity] NOAEL - general toxicity (PO) 4 mg/kg bw/day (nominal)) (male) based on: Decreased body weight gain at 20 and 100 mg/kg bw/day. **F1 generation** NOAEL : 100 mg/kg bw/day (nominal) (male/female) based on: Viability, clinical signs, mortality, body weights, gross pathology **Overall reproductive toxicity** not specified Lowest effective dose / concentration Relation to other toxic effects:	2 (reliable with restrictions) key study experimental study **Test material** 13815-17-3 / 237-489-7; Tetraamminepalladium dichloride, (full information in **Annex II**). **Reference** **Török-Bathó M 2015**
rat (Wistar [rat]) male/female screening for reproductive / developmental toxicity - based on test type (migrated information)	**First parental generation (P0)** NOAEL - fertility/reproductive parameters (PO) 100 mg/kg bw/day (nominal))	2 (reliable with restrictions) key study read-across from supporting substance

oral: gavage Doses / Concentrations: 4 mg/kg bw/day Basis: other: nominal dose Doses / Concentrations: 20 mg/kg bw/day Basis: other: nominal dose Doses / Concentrations: 100 mg/kg bw/day Basis: other: nominal dose Vehicle: an aqueous ammonium-chloride buffer (NH4Cl/NH4OH) was selected as the vehicle. The vehicle allowed formulation of a stable solution of the test item, considered suitable for the study purpose. Exposure: Males were dosed for 28 days (14 days pre-mating and 14 days mating/post- mating period). They were then euthanized and subjected to necropsy examination. Females were dosed for 14 days pre-mating, for up to 7 days mating period, through gestation and up to and including the day before necropsy (at least 4 days post-partum dosing). The day of birth (viz. when parturition was complete) is defined as Day 0 post-partum. (Once daily) according to OECD Guideline 421 (Reproduction / Developmental Toxicity Screening Test)	(male/female) based on: reproductive function (sperm measures) [reproductive toxicity] ; reproductive performance [reproductive toxicity] NOAEL - general toxicity (PO) 100 mg/kg bw/day (nominal)) (female) based on: clinical signs [general toxicity] ; mortality [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] ; histopathology: neoplastic [general toxicity] NOAEL - general toxicity (PO) 4 mg/kg bw/day (nominal)) (male) based on: Decreased body weight gain at 20 and 100 mg/kg bw/day. **F1 generation** NOAEL : 100 mg/kg bw/day (nominal) (male/female) based on: Viability, clinical signs, mortality, body weights, gross pathology **Overall reproductive toxicity** not specified Lowest effective dose / concentration Relation to other toxic effects:	(structural analogue or surrogate) **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**). **Reference** **Török-Bathó M 2015**
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable to each of the category member substances.		

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 5.10. Studies on developmental toxicity

Method	Results	Remarks
rat (Wistar [rat]) oral: gavage Vehicle: an aqueous ammonium-chloride buffer (NH4Cl/NH4OH) was selected as the vehicle. The vehicle allowed formulation of a stable solution of the test item, considered suitable for the study purpose. Exposure: Males were dosed for 28 days (14 days pre-mating and 14 days mating/post- mating period). They were then euthanized and subjected to necropsy examination. Females were dosed for 14 days pre-mating, for up to 7 days mating period, through gestation and up to and including the day before necropsy (at least 4 days post-partum dosing). The day of birth (viz. when parturition was complete) is defined as Day 0 post-partum. (Once daily) according to OECD Guideline 421 (Reproduction / Developmental Toxicity Screening Test)	**Maternal animals:** NOAEL: 100 mg/kg bw/day (nominal) based on: (test mat.) **Fetuses:** Fetal abnormalities not specified NOAEL: 100 mg/kg bw/day (nominal) based on: (test mat.) **Overall developmental toxicity:** no Lowest effective dose / concentration: Relation to maternal toxicity:	2 (reliable with restrictions) key study read-across from supporting substance (structural analogue or surrogate) **Test material** 61495-96-3 / 262-819-1; Tetraamminepalladium diacetate, Form: liquid (full information in **Annex II**). **Reference** **Török-Bathó M 2015**
Justification for type of information: Within the category of tetraamminepalladium(II) compounds, data on three tetraamminepalladium(II) salts, the diacetate, dichloride, and hydrogen carbonate salts will be used to fill data gaps. Tetraamminepalladium(II) diacetate, dinitrate, dihydroxide and dichloride are the target substances within the group. In all substances covered, the palladium is in the 2+ oxidation state, co-ordinated to four neutral ammonia molecules (giving an overall 2+ charge on the complex). Thus, the difference in anion (acetate, nitrate, hydroxide, chloride or hydrogen carbonate) represents the only structural difference between the compounds in this group. As detailed in the read-across justification report (cfr IUCLID section 13), all the human health toxicity data included in the category member dossiers should be considered equally applicable to each of the category member substances.		
rat (Wistar [rat]) oral: gavage Vehicle: an aqueous ammonium-chloride buffer (NH4Cl/NH4OH) was selected as the vehicle. The vehicle allowed formulation of a stable solution of the test item, considered suitable for the study purpose. Exposure: Males were dosed for 28 days (14 days pre-mating and 14 days mating/post- mating period). They were then euthanized and subjected to necropsy examination. Females were dosed for 14 days pre-mating, for up to 7 days mating period, through gestation and up to and including the day before necropsy (at least 4 days post-partum dosing). The day of birth (viz. when parturition was complete) is defined as Day 0 post-partum. (Once daily) according to OECD Guideline 421 (Reproduction / Developmental Toxicity Screening Test)	**Maternal animals:** NOAEL: 100 mg/kg bw/day (nominal) based on: (test mat.) **Fetuses:** Fetal abnormalities not specified NOAEL: 100 mg/kg bw/day (nominal) based on: (test mat.) **Overall developmental toxicity:** no Lowest effective dose / concentration: Relation to maternal toxicity:	2 (reliable with restrictions) key study experimental study **Test material** 13815-17-3 / 237-489-7; Tetraamminepalladium dichloride, (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 421 reproduction and developmental toxicity screening study, to GLP, parental rats (12/sex/group) were administered tetraamminepalladium dichloride by gavage at 0 (in aqueous ammonium chloride), 4, 20 or 100 mg/kg bw/day. No adverse effects on the dams, reproductive parameters, or on development of offspring, were observed at any dose, resulting in a reproductive toxicity NOAEL of 100 mg/kg bw/day (Török-Bathó, 2015).

Value used for CSA (route: oral):
no adverse effect observed (NOAEL): 100mg/kg bw/day (subacute, rat [common rodent species])

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.

However, a reliable reproduction/developmental screening toxicity study in rats has been conducted with tetraamminepalladium dichloride. Tetraamminepalladium dichloride is considered to fall within the scope of the read-across category “tetraamminepalladium salts”. See IUCLID section 13 for full read-across justification report.

The potential of tetraamminepalladium dichloride to adversely affect the fertility and reproductive parameters of rats was investigated in a reproductive and developmental screening study conducted according to OECD Test Guideline 421 and to GLP. The test material was administered (in aqueous ammonium chloride buffer) by oral gavage. Males were dosed for 28 days (14 days pre-mating and 14 days mating/post mating). Females were dosed for 14 days pre-mating, for up to 7 days mating period, through gestation and up to and including the day before necropsy (at least 4 days post-partum dosing). Three dose groups (4, 20, and 100 mg/kg bw/day) and a control group were used, each containing 12 animals of each sex.

Parental (F0) animals were observed for clinical signs of toxicity throughout the study, with body weights and food consumption monitored. At necropsy, animals were subjected to external and internal macroscopic examinations for any abnormalities or pathological changes. Special attention was paid to the reproductive organs. The numbers of implantation sites and corpora lutea were recorded. Histopathological examination was performed on the ovaries, testes and epididymides of all animals in the control and high-dose groups, with special emphasis on the qualitative stages of spermatogenesis and histopathology of interstitial testicular structure. A number of reproductive indices were calculated from the collected data (including mating, fertility and gestation indices).

Effects on the glandular stomach (including discolouration, inflammation, and congestion) were seen in the high-dose animals, and likely reflect a local effect of treatment. These effects in the glandular stomach may have contributed to the significantly reduced body weight gain seen in males at 20 and 100 mg/kg bw/day. The no-observed-adverse-effect level (NOAEL) for systemic toxicity was considered to be 4 mg/kg bw/day.

No test item-related microscopic changes were noted in the reproductive organs, and there was no impact on fertility or on the measured reproductive parameters at any dose level. The NOAEL for reproductive toxicity was 100 mg/kg bw/day, the highest dose tested (Török-Bathó, 2015).

Justification for selection of Effect on fertility via oral route:
Reliable GLP study, conducted according to OECD guidelines, and the only reproduction/developmental toxicity study available.

Developmental toxicity

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

In an OECD Test Guideline 421 reproduction and developmental toxicity screening study, to GLP, parental rats (12/sex/group) were administered tetraamminepalladium dichloride by gavage at 0 (in aqueous ammonium chloride), 4, 20 or 100 mg/kg bw/day. No adverse effects on the mothers, on reproductive parameters, or on development of offspring, were observed at any dose, resulting in a developmental toxicity NOAEL of 100 mg/kg bw/day (Török-Bathó, 2015).

Value used for CSA (route: oral):
no adverse effect observed (NOAEL): 100mg/kg bw/day (subacute; rat [common rodent species])

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.

However, a reliable reproduction/developmental screening toxicity study in rats has been conducted with tetraamminepalladium dichloride. Tetraamminepalladium dichloride is considered to fall within the scope of the read-across category “tetraamminepalladium salts”. See IULCID section 13 for full read-across justification report.

The potential of a solution of tetraamminepalladium dichloride to adversely affect the development of rat pups was investigated in a reproductive and developmental screening study conducted according to OECD Test Guideline 421, and to GLP. The test material was administered (in aqueous ammonium chloride buffer) by oral gavage. Males were dosed for 28 days (14 days pre-mating and 14 days mating/post mating). Females were dosed for 14 days pre-mating, for up to 7 days mating period, through gestation and up to and including the day before necropsy (at least 4 days post-partum dosing). Three dose groups (4, 20, and 100 mg/kg bw/day) and a

control group were used, each containing 12 animals of each sex.

Parental (F0) animals were observed for clinical signs of toxicity throughout the study, with body weights and food consumption monitored. At necropsy, animals were subjected to external and internal macroscopic examinations for any abnormalities or pathological changes. Special attention was paid to the reproductive organs. The numbers of implantation sites and corpora lutea were recorded. Histopathologic examination was performed on the ovaries, testes and epididymides of all animals in the control and high-dose groups, with special emphasis on the qualitative stages of spermatogenesis and histopathology of interstitial testicular structure. On postnatal day 4, pups were carefully examined for gross abnormalities at necropsy.

There were no signs of maternal toxicity or developmental toxicity effects at any dose level. In conclusion, under the conditions of this study, the NOAEL for developmental toxicity was considered to be 100 mg/kg bw/day (the highest tested dose) (Török-Bathó, 2015).

Justification for selection of Effect on developmental toxicity: via oral route:
Reliable 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 screening assay with tetraamminepalladium dichloride. As such, classification for reproductive 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

No relevant information available.

5.10.2. Human information

No relevant information available.

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	adverse effect observed (LD50): 933mg/kg bw
Acute toxicity	dermal	no adverse effect observed
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	adverse effect observed (sensitising)
Sensitisation	resp. tract	no study available
Repeated dose toxicity	oral	adverse effect observed (NOAEL): 4mg/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 adverse effect observed (negative)
Reproductive toxicity: effects on fertility	oral	no adverse effect observed (NOAEL): 100mg/kg bw/day (subacute; rat [common rodent species])
Reproductive toxicity: effects on fertility	dermal	no study available
Reproductive toxicity:	inhalation	no study available

effects on fertility		
Reproductive toxicity: developmental toxicity	oral	no adverse effect observed (NOAEL): 100mg/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	DNEL (Derived No Effect Level) 0.26mg/m³	repeated dose toxicity (Oral)
Inhalation	Systemic effects - Acute	no hazard identified	
Inhalation	Local effects - Long-term	medium hazard (no threshold derived)	sensitisation (skin)
Inhalation	Local effects - Acute	medium hazard (no threshold derived)	sensitisation (skin)
Dermal	Systemic effects - Long-term	DNEL (Derived No Effect Level) 0.36mg/kg bw/day	repeated dose toxicity (Oral)
Dermal	Systemic effects - Acute	no hazard identified	
Dermal	Local effects - Long-term	high hazard (no threshold derived)	sensitisation (skin)
Dermal	Local effects - Acute	high hazard (no threshold derived)	sensitisation (skin)
Eyes	Local effects	low hazard (no threshold derived)	

Inhalation Systemic effects - Long-term

DNEL derivation method: ECHA REACH Guidance

Modified dose descriptor starting point: NOAEC

See discussion section (Hazard via inhalation route: systemic effects following long-term exposure)

Overall Assessment Factor: 75

AF for dose response relationship: 1 (Default ECHA AF; NOAEL from a well-conducted reproductive/ developmental toxicity study; the highest dose was set at 100 mg/kg bw/day on the basis of a 14-day dose

range finding study (the aim was to induce toxic effects but no death or suffering at the highest dose and to achieve a NOAEL at the lowest dose))

AF for difference in duration of exposure: 6 (Default ECHA AF for subacute (28-day) to chronic extrapolation. Male animals were dosed for 28-days in total, while females received treatment for a longer period of time (incorporating the gestation period and proceeding up until postpartum day 4))

AF for interspecies differences (allometric scaling): 1 (Default ECHA AF for rat for toxicokinetic differences in metabolic rate (allometric scaling) is not required)

AF for other interspecies differences: 2.5 (Default ECHA AF for remaining toxicokinetic differences (not related to metabolic rate) and toxicodynamic differences)

AF for intraspecies differences: 5 (Default ECHA AF for (healthy) worker)

AF for the quality of the whole database: 1 (Default ECHA AF; the human health effects data are reliable and consistent, and confidence in the database is high. Read-across from the structurally-similar compounds, tetraamminepalladium dichloride and tetraamminepalladium hydrogen carbonate was used to fill the reproductive/developmental and repeated dose toxicity (oral) endpoints respectively. No AF is considered necessary for the use of read-across since the source substances both display a high degree of similarity to the target compound. Notably, the counter ions (acetate, chloride or hydrogen carbonate) are not anticipated to differentially influence the toxicity of the palladium(II) species. Moreover, the DNEL was derived on the basis of palladium itself)

AF for remaining uncertainties: 1 (Not required)

Further explanation on hazard conclusions:

See discussion section (Hazard via inhalation route: systemic effects following long-term exposure)

Inhalation Systemic effects - Acute

Further explanation on hazard conclusions:

See discussion section (Hazard via inhalation route: systemic effects following acute exposure)

Inhalation Local effects - Long-term

Further explanation on hazard conclusions:

See discussion section (Hazard via inhalation route: local effects following long-term exposure)

Inhalation Local effects - Acute

Further explanation on hazard conclusions:

See discussion section (Hazard via inhalation route: local effects following acute exposure)

Dermal Systemic effects - Long-term

DNEL derivation method: ECHA REACH Guidance

Modified dose descriptor starting point: NOAEL

See discussion section (Hazard via dermal route: systemic effects following long-term exposure)

Overall Assessment Factor: 75

AF for dose response relationship: 1 (Default ECHA AF; NOAEL from a well-conducted

reproductive/developmental toxicity study; the highest dose was set at 100 mg/kg bw/day on the basis of a 14-day dose range finding study (the aim was to induce toxic effects but no death or suffering at the highest dose and to achieve a NOAEL at the lowest dose))

AF for difference in duration of exposure: 6 (Default ECHA AF for subacute (28-day) to chronic extrapolation. Male animals were dosed for 28-days in total, while females received treatment for a longer period of time (incorporating the gestation period and proceeding up until postpartum day 4))

AF for interspecies differences (allometric scaling): 1 (The default ECHA AF of 4 for rat for toxicokinetic differences in metabolic rate (allometric scaling) is considered unnecessary as the compound is inorganic and is consequently not metabolised to any relevant extent. Moreover, ECHA guidance notes that "allometric scaling is an empirical approach for interspecies extrapolation of various kinetic processes generally applicable to substances which are renally excreted", while systemically available palladium is excreted predominantly via the biliary/faecal route)

AF for other interspecies differences: 2.5 (Default ECHA AF for remaining toxicokinetic differences (not related to metabolic rate) and toxicodynamic differences)

AF for intraspecies differences: 5 (Default ECHA AF for (healthy) worker)

AF for the quality of the whole database: 1 (Default ECHA AF; the human health effects data are reliable and consistent, and confidence in the database is high. Read-across from the structurally-similar compounds, tetraamminepalladium dichloride and tetraamminepalladium hydrogen carbonate was used to fill the reproductive/developmental and repeated dose toxicity (oral) endpoints respectively. No AF is considered necessary for the use of read-across since the source substances both display a high degree of similarity to the target compound. Notably, the counter ions (acetate, chloride or hydrogen carbonate) are not anticipated to differentially influence the toxicity of the palladium (II) species. Moreover, the DNEL was derived on the basis of palladium itself)

AF for remaining uncertainties: 1 (Not required)

Further explanation on hazard conclusions:

See discussion section (Hazard via dermal route: systemic effects following long-term exposure)

Dermal Systemic effects - Acute

Further explanation on hazard conclusions:

See discussion section (Hazard via dermal route: systemic effects following acute exposure)

Dermal Local effects - Long-term

Further explanation on hazard conclusions:

See discussion section (Hazard via dermal route: local effects following long-term exposure)

Dermal Local effects - Acute

Further explanation on hazard conclusions:

See discussion section (Hazard via dermal route: local effects following acute exposure)

Discussion:

Hazard via inhalation route: systemic effects following long-term exposure

Justification for route to route extrapolation

As no relevant data on effects of repeated exposure to tetraamminepalladium diacetate in humans or laboratory

animals are available, route-to-route extrapolation to calculate an inhalation DNEL from a reproductive/developmental oral toxicity study on a member of the “tetraamminepalladium salts” category, tetraamminepalladium dichloride, was considered a suitable alternative (particularly as first pass effects are not expected to be significant for an inorganic compound).

The oral NOAEL for tetraamminepalladium dichloride was 4 mg/kg bw/day. This equates to NOAELs of 1.76 and 5.45 mg/kg bw/day for palladium and tetraamminepalladium diacetate, respectively (based on MWt ratios).

In the absence of data allowing quantitative comparison between absorption following oral and inhalation exposure, this derivation utilised the REACH default assumption that the absorption percentage for the oral route is half that of the inhalation route, and a default factor of 2 is proposed for absorption differences in the case of oral-to-inhalation extrapolation.

Expressed as tetraamminepalladium diacetate the corrected inhalatory NOAEC (worker, 8 h exposure/day) = oral NOAEL*(1/sRv[rat])*(ABS[oral-rat]/ABS[inh-human]) *(sRV[human]/wRV) = 5.45 mg/kg bw/day*(1/0.38 m3/kg bw/day)*(1/2)*(6.7 m3 [8h]/10 m3 [8h]) = 4.80 mg/m3.

It is noted that the standard respiratory rate conversion figure (0.38 m3/kg bw/day) already incorporates a factor of 4 for allometric scaling from rat to human. An assessment factor (AF) for allometric scaling is not considered to be justified in this scenario, given that the metabolism of inorganic metal cations is conventionally assumed not to occur to any relevant extent. Moreover, ECHA guidance notes that “allometric scaling is an empirical approach for interspecies extrapolation of various kinetic processes generally applicable to substances which are renally excreted, but not to substances which are highly extracted by the liver and excreted in the bile. It appears that species differences in biliary excretion and glucuronidation are independent of caloric demand (Walton et al. 2001)” (ECHA, 2012a). Oral toxicokinetic studies have demonstrated that systemically available palladium is excreted predominantly via the biliary/faecal route.

It is therefore appropriate to increase the corrected inhalatory NOAEC by a factor of 4.

Dose descriptor starting point (after route to route extrapolation) = Corrected inhalatory NOAEC (worker, 8 h exposure/day)*4 = 4.80*4 = 19.2 mg/m3.

Justification and comments

In a OECD Test Guideline 421 reproductive/developmental toxicity study, conducted according to GLP, rats (12/sex/group) received a solution of tetraamminepalladium dichloride by gavage at doses of 0, 4, 20, or 100 mg/kg bw/day for at least 28 days (males were dosed for 28-days in total, while females received treatment for a longer period of time [incorporating the gestation period and proceeding up until postpartum day 4, i.e. around 7-8 weeks]).Effects on the glandular stomach were seen in the high-dose animals, and likely reflect a local effect of treatment. These effects in the glandular stomach may have contributed to the significantly reduced body weight gain seen in males at 20 and 100 mg/kg bw/day (growth of females was unaffected).The NOAEL for systemic toxicity was 4 mg/kg bw/day on the basis of reduced growth in males at 20 and 100 mg/kg bw/day. No test item-related microscopic changes were noted in the reproductive organs. Moreover, no effects on reproductive parameters or indications of maternal/foetal toxicity were observed at any dose level (Török-Bathó,

2015). The possible limitations of this screening study, as reassurance of an absence of reproductive effects, are acknowledged. ECHA (2012a) guidance recommends “application of an additional assessment factor of 2 to 5, decided on a case-by-case basis that should account for the limitations of this study”. Even applying the most conservative of these (i.e. an additional AF of 5) results in a DNEL higher than that derived for repeated dose effects.

In a guideline (EU Method B.7) 28-day gavage toxicity study on a different source substance, tetraamminepalladium hydrogen carbonate, a slightly higher NOAEL of 15 mg/kg bw/day was obtained based on microscopic changes in the spleen in high-dose animals (150 mg/kg bw/day) (Wragg et al., 1997).

The slightly lower NOAEL of 4 mg/kg bw/day for repeated dose effects was taken as the health-precautionary critical point of departure for calculating the long-term systemic DNELs for tetraamminepalladium diacetate, and is considered protective of fertility and developmental toxicity.

The DNEL (0.26 mg/m3) equates to a palladium exposure of 0.08 mg/m3.

Hazard via inhalation route: systemic effects following acute exposure

Justification and comments

DNELs for acute toxicity should be calculated if an acute toxicity hazard, leading to classification and labelling (i.e. under EU CLP regulations) has been identified and there is a potential for high peak exposures (this is only usually relevant for inhalation exposures).

There are no data in relation to acute inhalation exposure to tetraamminepalladium diacetate. In a guideline (OECD TG 401) acute oral toxicity study in rats, on the structurally-related compound tetraamminepalladium hydrogen carbonate, an LD50 value of 933 mg/kg bw (females) was obtained (Allen, 1995a). This compound is classified in Category 4 for acute oral toxicity according to CLP. Accordingly, an identical classification was adopted for tetraamminepalladium diacetate. An oral N(L)OAEL (for sub-lethal effects) could be modified into an inhalation N(L)OAEC using route-to-route extrapolation. However, ECHA (2012a) guidance on DNEL calculation notes that this “procedure introduces significant uncertainties especially in relation to what inhalation time-frame this extrapolated N(L)OAEC would represent, and the procedure is therefore discouraged”.

Palladium diacetate has the same organic component as tetraamminepalladium diacetate, and has a very low QSAR-predicted vapour pressure (0.00239 Pa at 25°C; USEPA, 2010), indicating that only a small proportion of the latter substance may be available for inhalation as a vapour. Particle size distribution testing was waived as the substance is marketed in a non solid or granular form (as a solution). Accordingly, inhalation is not considered to be a significant route of exposure.

Further, setting acute DNELs is unnecessary, based on the high-level principle referenced in ECHA (2012a). This criterion states that “As a rule of thumb, a DNELacute should be set for acutely toxic substances if actual

peak exposure levels significantly exceed the long-term DNEL". This is typically inferred to mean several fold exceedance for task-based (e.g. 15 minute TWA) situations. The foreseeable industrial situations are highly unlikely to result in airborne peak exposures well above 0.26 mg/m3 as these would not be tolerated in the workplaces (due to the general standards applicable to control of particulates). Consequently, no worker-DNEL for acute systemic toxicity has been calculated.

"A qualitative risk characterisation for this endpoint could be performed for substances of very high or high acute toxicity classified in Category 1, 2 and 3 according to CLP…. when the data are not sufficiently robust to allow the derivation of a DNEL" (ECHA, 2012b). However, tetraamminepalladium diacetate is classified in Category 4 according to CLP, so a qualitative assessment is not required.

Hazard via inhalation route: local effects following long-term exposure

Justification and comments

There are no data in relation to respiratory tract irritation or sensitisation in humans or laboratory animals. Consequently, no worker-DNELs for respiratory tract irritation/corrosion or sensitisation have been calculated.

However, according to ECHA (2012b) guidance "since sensitisation is essentially systemic in nature, it is important for the purposes of risk management to acknowledge that skin sensitisation may be acquired by other routes of exposure than dermal. There is therefore a need for cautious use of known contact allergens in products to which consumers or workers may be exposed by inhalation". Tetraamminepalladium diacetate is classified as an extreme/strong skin sensitiser, on the basis of read-across from tetraamminepalladium dichloride and tetraamminepalladium hydrogen carbonate. Therefore, consider recommended Risk Management Measures/Operational Conditions (RMMs/OCs) in Table E.3-1 of ECHA (2012b).

Hazard via inhalation route: local effects following acute exposure

Justification and comments

There are no data in relation to respiratory tract irritation or sensitisation in humans or laboratory animals. Consequently, no worker-DNEL for acute local effects in the respiratory tract has been calculated.

However, according to ECHA (2012b) guidance "since sensitisation is essentially systemic in nature, it is important for the purposes of risk management to acknowledge that skin sensitisation may be acquired by other routes of exposure than dermal. There is therefore a need for cautious use of known contact allergens in products to which consumers or workers may be exposed by inhalation". Tetraamminepalladium diacetate is classified as an extreme/strong skin sensitiser, on the basis of read-across from tetraamminepalladium dichloride and tetraamminepalladium hydrogen carbonate. Therefore, consider RMMs/OCs in Table E.3-1 of ECHA (2012b).

Hazard via dermal route: systemic effects following long-term exposure

Justification for route to route extrapolation

As no relevant data on effects of repeated exposure to tetraamminepalladium diacetate in humans or laboratory animals are available, route-to-route extrapolation to calculate a dermal DNEL from a reproductive/developmental oral toxicity study on a member of the “tetraamminepalladium salts” category, tetraamminepalladium dichloride was considered a suitable alternative (particularly as first pass effects are not expected to be significant for inorganic compounds).

The oral NOAEL for tetraamminepalladium dichloride was 4 mg/kg bw/day. This equates to NOAELs of 1.76 and 5.45 mg/kg bw/day for palladium and tetraamminepalladium diacetate, respectively (based on MWt ratios).

Estimation of dermal absorption is based on relevant available information (mainly water solubility, molecular weight and log Pow) and expert judgement. Tetraamminepalladium diacetate, with anticipated high water solubility, may be unable to cross the lipid-rich environment of the stratum corneum, especially given the lack of skin irritation potential, predicted based on the absence of such potential in the structurally related compounds tetraamminepalladium dichloride and tetraamminepalladium hydrogen carbonate (skin irritation potential could, in theory, disrupt skin barrier function). Further, dermal penetration is likely to be limited by the poor lipophilicity of the organic portion of the molecule, as represented by acetic acid (log Pow of -0.17; Hansch, 1995), for absorption through the skin. In spite of this, in the light of the limited available experimental data, ECHA guidance indicates a default value of 100% dermal absorption (ECHA, 2014). However, 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). Given the low penetration expected from metals, and the high water solubility (and, thus, low expected lipophilicity), 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 tetraamminepalladium diacetate.

In the absence of absorption data for the starting route, a pragmatic assumption has to be made (i.e. a limited absorption for the oral route). In line with REACH guidance, it is considered that the absorption percentage for the oral route is 50% (instead of 100%).

Accordingly, use of an oral benchmark to assess a dermal exposure necessitates an increase in the starting point by a corrective factor of 5 to account for the difference in absorption between these two routes.

Dose descriptor starting point (after route to route extrapolation) = NOAEL*(ABS[oral-rat]/ABS[der-human]) = 5.45 mg/kg bw/day*(50%/10%) = 27.2 mg/kg bw/day.

Justification and comments

In a OECD Test Guideline 421 reproductive/developmental toxicity study, conducted according to GLP, rats (12/sex/group) received a solution of tetraamminepalladium dichloride by gavage at doses of 0, 4, 20, or 100 mg/kg bw/day for at least 28 days (males were dosed for 28-days in total, while females received treatment for a longer period of time [incorporating the gestation period and proceeding up until postpartum day 4, i.e. around 7-8 weeks. Effects on the glandular stomach were seen in the high-dose animals, and likely reflect a local effect of treatment. These effects in the glandular stomach may have contributed to the significantly reduced body weight gain seen in males at 20 and 100 mg/kg bw/day (growth of females was unaffected).The NOAEL for

systemic toxicity was 4 mg/kg bw/day on the basis of reduced growth in males at 20 and 100 mg/kg bw/dayNo test item-related microscopic changes were noted in the reproductive organs. Moreover, no effects on reproductive parameters or indications of maternal/foetal toxicity were observed at any dose level (Török-Bathó, 2015). The possible limitations of this screening study, as reassurance of an absence of reproductive effects, are acknowledged. ECHA (2012a) guidance recommends "application of an additional assessment factor of 2 to 5, decided on a case-by-case basis that should account for the limitations of this study". Even applying the most conservative of these (i.e. an additional AF of 5) results in a DNEL higher than that derived for repeated dose effects.

In a guideline (EU Method B.7) 28-day gavage toxicity study on a different source substance, tetraamminepalladium hydrogen carbonate, a slightly higher NOAEL of 15 mg/kg bw/day was obtained based on microscopic changes in the spleen in high-dose animals (150 mg/kg bw/day) (Wragg et al., 1997).

The slightly lower NOAEL of 4 mg/kg bw/day for repeated dose effects was taken as the health-precautionary critical point of departure for calculating the long-term systemic DNELs for tetraamminepalladium diacetate, and is considered protective of fertility and developmental toxicity.

The DNEL (0.36 mg/kg bw/day) equates to a palladium exposure of 0.12 mg/kg bw/day.

Hazard via dermal route: systemic effects following acute exposure

Justification and comments

DNELs for acute toxicity should be calculated if an acute toxicity hazard, leading to classification and labelling (i.e. under EU CLP regulations) has been identified and there is a potential for high peak exposures (this is only usually relevant for inhalation exposures).

No acute dermal toxicity study was conducted on tetraamminepalladium diacetate. In a guideline (OECD TG 402) acute dermal toxicity study in rats, on the structurally-related compound tetraamminepalladium hydrogen carbonate, the LD50 value was found to exceed 2000 mg/kg bw (males and females) (Allen, 1997a). This compound is not classified for acute dermal toxicity under CLP. Accordingly, an identical lack of classification was expected for tetraamminepalladium diacetate.

As tetraamminepalladium diacetate is not classified for acute dermal toxicity, no worker-DNEL for acute systemic toxicity following dermal exposure has been calculated.

Hazard via dermal route: local effects following long-term exposure

Justification and comments

In guideline (OECD TG 404) skin irritation studies in rabbits, the structurally-related compounds tetraamminepalladium dichloride and tetraamminepalladium hydrogen carbonate produced no evidence of skin irritation (Allen, 1995b; Driscoll, 1981). These compounds are not classified for skin irritation under CLP. Accordingly, an identical lack of classification was expected for tetraamminepalladium diacetate.

In other guideline (OECD TG 406) studies, the structurally-related compounds tetraamminepalladium dichloride and tetraamminepalladium hydrogen carbonate induced skin sensitisation in the guinea pig maximisation test (GPMT). Evidence of sensitisation was observed in at least 60% of the treated animals in both cases (Allen, 1997b, 2000). These compounds are classified for skin sensitisation as Category 1A, under CLP. Accordingly, an identical classification was adopted for tetraamminepalladium diacetate.

According to ECHA (2012b) guidance “extreme and strong skin sensitisers (classified in Sub-category 1A in CLP) are allocated to the high hazard band on the basis that exposure to such potent skin sensitising substances should be strictly contained and dermal contact avoided”.

Therefore, consider recommended RMMs/OCs in Table E.3-1 of ECHA (2012b).

Hazard via dermal route: local effects following acute exposure

Justification and comments

In guideline (OECD TG 404) skin irritation studies in rabbits, the structurally-related compounds tetraamminepalladium dichloride and tetraamminepalladium hydrogen carbonate produced no evidence of skin irritation (Allen, 1995b; Driscoll, 1981). These compounds are not classified for skin irritation under CLP. Accordingly, an identical lack of classification was expected for tetraamminepalladium diacetate.

In other guideline (OECD TG 406) studies, the structurally-related compounds tetraamminepalladium dichloride and tetraamminepalladium hydrogen carbonate induced skin sensitisation in the GPMT. Evidence of sensitisation was observed in at least 60% of the treated animals in both cases (Allen, 1997b, 2000). These compounds are classified for skin sensitisation as Category 1A, under CLP. Accordingly, an identical classification was adopted for tetraamminepalladium diacetate.

According to ECHA (2012b) guidance “extreme and strong skin sensitisers (classified in Sub-category 1A in CLP) are allocated to the high hazard band on the basis that exposure to such potent skin sensitising substances should be strictly contained and dermal contact avoided”.

Therefore, consider recommended RMMs/OCs in Table E.3-1 of ECHA (2012b).

Hazard for the eyes

Justification and comments

In a guideline (OECD TG 405) eye irritation study, the structurally-related compound tetraamminepalladium dichloride produced severe eye irritation in rabbits (Driscoll & Collier, 1981). The compound is classified in Category 2 under EU CLP. Accordingly, an identical classification was adopted for tetraamminepalladium diacetate.

No dose-response data was available from which to derive a DNEL, therefore a qualitative assessment was considered appropriate. Substances classified for serious eye irritation (Category 2 in CLP) should be allocated to the "low hazard band on the basis that effects due to such moderately irritant substances are anticipated at higher concentrations when compared to the high and moderate hazard band irritants". Therefore, consider recommended RMMs/OCs in Table E.3-1 of ECHA (2012b).

Table 5.13. Hazard conclusions for the general population

Route	Type of effect	Hazard conclusion	Most sensitive endpoint
Inhalation	Systemic effects - Long-term	hazard unknown but no further hazard information necessary as no exposure expected	
Inhalation	Systemic effects - Acute	hazard unknown but no further hazard information necessary as no exposure expected	
Inhalation	Local effects - Long-term	hazard unknown but no further hazard information necessary as no exposure expected	
Inhalation	Local effects - Acute	hazard unknown but no further hazard information necessary as no exposure expected	
Dermal	Systemic effects - Long-term	hazard unknown but no further hazard information necessary as no exposure expected	
Dermal	Systemic effects - Acute	hazard unknown but no further hazard information necessary as no exposure expected	
Dermal	Local effects - Long-term	hazard unknown but no further hazard information necessary as no exposure expected	
Dermal	Local effects - Acute	hazard unknown but no further hazard information necessary as no exposure expected	
Oral	Systemic effects - Long-term	hazard unknown but no further hazard information necessary as no exposure expected	
Oral	Systemic effects -	hazard unknown but no further	

	Acute	hazard information necessary as no exposure expected	
Eyes	Local effects	low hazard (no threshold derived)	

Inhalation Systemic effects - Long-term

Further explanation on hazard conclusions:

See discussion section

Inhalation Systemic effects - Acute

Further explanation on hazard conclusions:

See discussion section

Inhalation Local effects - Long-term

Further explanation on hazard conclusions:

See discussion section

Inhalation Local effects - Acute

Further explanation on hazard conclusions:

See discussion section

Dermal Systemic effects - Long-term

Further explanation on hazard conclusions:

See discussion section

Dermal Systemic effects - Acute

Further explanation on hazard conclusions:

See discussion section

Dermal Local effects - Long-term

Further explanation on hazard conclusions:

See discussion section

Dermal Local effects - Acute

Further explanation on hazard conclusions:

See discussion section

Oral Systemic effects - Long-term

Further explanation on hazard conclusions:

See discussion section

Oral Systemic effects - Acute

Further explanation on hazard conclusions:

See discussion section

Discussion:

DNELs have been derived only for workers, not for consumers/general population. During assessment of the identified uses for tetraamminepalladium diacetate, no uses have been identified in which consumers are exposed to tetraamminepalladium diacetate. In all uses with potential consumer exposure due to service life of articles, tetraamminepalladium diacetate is chemically transformed into another substance before reaching the consumers, and the subsequent lifecycle steps after this transformation of tetraamminepalladium diacetate 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 tetraamminepalladium diacetate 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: Tetraamminepalladium (2+) diacetate

Related composition: Tetraamminepalladium(2+) diacetate (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 according to UN Manual of Tests and Criteria: Test N.1 (Test method for readily combustible solids)	Evaluation of results: not classified based on GHS criteria Study results: Flammable gasses (lower and upper explosion limits): Aerosols: Flammable solids: burning rate test: preliminary screening test (substance does not ignite and propagate combustion either by burning with flame or smouldering along 200 mm of the powder train within the 2 minutes test period) Pyrophoric solids: Pyrophoric liquid: Self-heating substances/mixtures: Substances/ mixture which in contact with water emit flammable gases: Remarks: The sample of Tetraamminepalladium (II) acetate could not be ignited with the gas burner (burning time 2 min) at the preliminary screening test.	1 (reliable without restriction) key study experimental study **Test material** Tetraamminepalladium (II) acetate, Form: solid: particulate/powder (full information in **Annex II**). **Reference** **Michael-Schulz H. 2016**

Discussion

The following information is taken into account for any hazard / risk assessment:
Flammability.
Key value for chemical safety assessment: Flammability: not classified

Tetraamminepalladium (II) acetate does not fulfil the criteria of Class 4.1 ‘Flammable Solids’ of the TGD and the Hazard Class ‘Flammable Solids’ of the Regulation (EC) No 1272/2008 (CLP) and GHS as the test item could not be ignited with the gas burner (burning time 2 min) in the preliminary screening test.

Additional information:

The flammability of Tetraamminepalladium (II) acetate was determined in a study according the UN-Test N.1 (Michael-Schulz 2016). This is a non-GLP, guideline study and is considered suitable for use as the key study for this endpoint.

Flash Point

No relevant information available.
Data waiving: see CSR section 1.3 Physicochemical properties.

Classification according to GHS

Name: Tetraamminepalladium (2+) diacetate

Related composition: Tetraamminepalladium(2+) diacetate (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:

Tetraamminepalladium (II) acetate could not be ignited at the preliminary screening test and therefore the test item does not fulfil the criteria of Class 4.1 ‘Flammable Solids’ of the TGD and the Hazard Class ‘Flammable Solids’ of the Regulation (EC) No 1272/2008 (CLP) and GHS.

6.3. Oxidising potential

No relevant information available.
Data waiving: see CSR section 1.3 Physicochemical properties.

Classification according to GHS

Name: Tetraamminepalladium (2+) diacetate

Related composition: Tetraamminepalladium(2+) diacetate (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

7. ENVIRONMENTAL HAZARD ASSESSMENT

7.1. Aquatic compartment (including sediment)

7.1.1. Fish

7.1.1.1. Short-term toxicity to fish

The results are summarised in the following table:

Table 7.1. Short-term effects on fish

Method	Results	Remarks
Oncorhynchus mykiss (previous name: Salmo gairdneri) freshwater short-term toxicity to fish according to OECD Guideline 203 (Fish, Acute Toxicity Test)	LC50 (96h): 154 µg/L element - palladium (meas. (geom. mean)) based on: mortality (95% CL 102 - 223) LC50 (96h): 306 µg/L test mat. - diamminedichloropalladium (meas. (geom. mean)) based on: mortality (95% CL 203 - 443) LC10 (96h): 180 µg/L test mat. - diamminedichloropalladium (meas. (geom. mean)) based on: mortality LC10 (96h): 90.4 µg/L element - palladium (meas. (geom. mean)) based on: mortality	1 (reliable without restriction) key study experimental study **Test material** 14323-43-4 / 238-269-3, Form: solid: particulate/powder - migrated information: powder (full information in **Annex II**). **Reference** **Teigeler 2012**
Oncorhynchus mykiss (previous name: Salmo gairdneri) freshwater short-term toxicity to fish according to OECD Guideline 203 (Fish, Acute Toxicity Test)	LC50 (96h): 0.191 mg/L element - palladium (nominal) based on: mortality (Concentration expressed as palladium, determined based on molecular weight coversion) LC50 (96h): 0.53 mg/L test mat. (nominal) based on: mortality (95% Confidence Limits of 0.44-0.64 mg/l) NOEC (96h): >=0.32 mg/L test mat. (nominal) based on: mortality	2 (reliable with restrictions) key study experimental study **Test material** 134620-00-1 / 134620-00-1; Tetrammine Palladium Hydrogen Carbonate, (full information in **Annex II**). **Reference** **Wetton PM 1997**
short-term toxicity to fish		3 (not reliable) disregarded due to major methodological deficiencies experimental study **Test material** Dihydrogen

		tetrachloropalladate, (full information in **Annex II**). **Reference** **Pawlowski, S and Wydra, V 2005**

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

The results are summarised in the following table:

Table 7.2. Short-term effects on aquatic invertebrates

Method	Results	Remarks
Daphnia magna freshwater static according to OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test)	EC50 (48h): 35.19 µg/L element - palladium (meas. (arithm. mean)) based on: mobility EC50 (48h): 69.91 µg/L test mat. - Diamminedichloropalladium (meas. (arithm. mean)) based on: mobility NOEC (48h): 20.52 µg/L element - palladium (meas. (arithm. mean)) based on: mobility NOEC (48h): 40.77 µg/L test mat. - Diamminedichloropalladium (meas. (arithm. mean)) based on: mobility LOEC (48h): 40.1 µg/L element - palladium (meas. (arithm. mean)) based on: mobility LOEC (48h): 79.67 µg/L test mat. - Diamminedichloropalladium (meas. (arithm. mean)) based on: mobility	1 (reliable without restriction) key study experimental study **Test material** Diamminedichloropalladium (II), Form: solid: particulate/powder - migrated information: powder (full information in **Annex II**). **Reference** **Schlechtriem 2012**
Daphnia magna freshwater static according to Commission Directive 92/69/EEC Annex Part C, C.2; OECD Guideline 202; OECD Guidance Document for Testing and Assessment, No.23 (Aquatic Toxicity Testing of Difficult Substances and Mixtures).	EC50 (48h): 0.021 mg/L element (nominal) based on: swimming or mortality EC50 (48h): 0.107 mg test item / L test mat. (nominal) based on: swimming or mortality (95% confidence values 0.092-0.125 mg test item/L) EC0 (48h): 0.03 mg test item / L; test mat. (nominal) based on: swimming or mortality EC100 (48h): 0.263 mg test item / L; test mat. (nominal) based on: swimming or mortality NOEC (48h): 0.045 mg test item / L; test mat. (nominal) based on: swimming or mortality LOEC (48h): 0.097 mg test item / L; test mat. (nominal) based on: swimming or mortality	1 (reliable without restriction) key study experimental study **Test material** Dihydrogen tetrachloropalladate (II); palladium(4+) tetrachloride / 16970-55-1 / 241-047-9, Form: liquid (full information in **Annex II**). **Reference** **Moll and Wydra**

		2005
Daphnia magna freshwater static according to OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test)	EC50 (48h): 46.5 µg/L element (meas. (TWA)) based on: immobility EC50 (24h): 0.29 mg/L test mat. (nominal) based on: Immobility (95% Confidence Limits: 0.26 - 0.33 mg/l) EC50 (48h): 0.22 mg/L test mat. (nominal) based on: Immobility (95% Confidence Limits: 0.20 - 0.25 mg/l) EC50 (24h): 0.18 mg/L test mat. (meas. (TWA)) based on: Immobility (95% Confidence Limits: 0.16 - 0.20) EC50 (48h): 0.13 mg/L test mat. (meas. (TWA)) based on: Immobility (95% Confidence Limits: 0.11 - 0.14) NOEC (24h): 0.18 mg/L test mat. (nominal) based on: Immobility NOEC (48h): 0.1 mg/L test mat. (nominal) based on: Immobility NOEC (24h): 0.12 mg/L test mat. (meas. (TWA)) based on: Immobility NOEC (48h): 0.06 mg/L test mat. (meas. (TWA)) based on: Immobility	2 (reliable with restrictions) key study experimental study **Test material** 134620-00-1 / 134620-00-1; Tetrammine Palladium Hydrogen Carbonate, (full information in **Annex II**). **Reference** **Wetton PM 1997**

7.1.2.2. Long-term toxicity to aquatic invertebrates

The results are summarised in the following table:

Table 7.3. Long-term effects on aquatic invertebrates

Method	Results	Remarks
Daphnia magna freshwater long-term toxicity to aquatic invertebrates according to OECD Guideline 211 (Daphnia magna Reproduction Test)	NOEC (21d): >=14.3 µg/L element - Palladium (meas. (TWA)) based on: mortality - growth, reproduction and time to first brood NOEC (21d): >=28.4 µg/L test mat. - DDP (meas. (TWA)) based on: mortality - growth, reproduction and time to first brood	1 (reliable without restriction) key study experimental study **Test material** 14323-43-4 / 238-269-3; Diamminedichloropalladium (II), Form: solid: particulate/powder - migrated information: powder (full information in **Annex II**). **Reference** **Simon 2014**
Daphnia magna freshwater long-term toxicity to aquatic invertebrates according to OECD Guideline 211 (Daphnia magna Reproduction Test)	EC10 (21d): 35.7 µg/L element (dissolved fraction) - Pd (meas. (TWA)) based on: reproduction - reproduction determined as offspring per survived parent (- 95%CI: 22.3-45.0 µg Pd/L)	1 (reliable without restriction) key study experimental study

	NOEC (21d): 42.7 µg/L element (dissolved fraction) - Pd (meas. (TWA)) based on: reproduction - offspring per survived parent (’reproduction), immobility, length, age of first reproduction and intrinsic rate NOEC (21d): 102 µg/L test mat. (dissolved fraction) - Tetraamminepalladium dichloride (meas. (TWA)) based on: reproduction - offspring per survived parents (’reproduction’), immobility, length, age of first reproduction and intrinsic rate EC10 (21d): 84.9 µg/L test mat. (dissolved fraction) (meas. (TWA)) based on: reproduction - reproduction determined as offspring per survived parent (- 95% CI: 53-107 µg TI/L)	**Test material** Tetraamminepalladium (II) chloride, Form: not specified (full information in **Annex II**). **Reference** **Brüggemann M 2019**

7.1.3. Algae and aquatic plants

The results are summarised in the following table:

Table 7.4. Effects on algae and aquatic plants

Method	Results	Remarks
Pseudokirchneriella subcapitata (previous names: Raphidocelis subcapitata, Selenastrum capricornutum) (algae) freshwater toxicity to aquatic algae and cyanobacteria according to OECD Guideline 201 (Alga, Growth Inhibition Test) [before 23 March 2006]	EC10 (72h): 1.88 µg/L element - Palladium (meas. (geom. mean)) based on: growth rate (95% CL 1.29 - 2.24) 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) 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	1 (reliable without restriction) key study experimental study **Test material** 14323-43-4 / 238-269-3, Form: solid: particulate/powder - migrated information: powder (full information in **Annex II**). **Reference** **Wenzel 2012**

	- 4.45) EC10 (72h): 1.43 µg/L element - Palladium (meas. (geom. mean)) based on: yield (95% CL 1.26 - 1.59)	
Desmodesmus subspicatus (previous name: Scenedesmus subspicatus) (algae) freshwater toxicity to aquatic algae and cyanobacteria according to EU Method C.3 (Algal Inhibition test) ; according to OECD Guideline 201 (Alga, Growth Inhibition Test) [before 23 March 2006]	EC50 (72h): <8.5 µg/L element (estimated) based on: biomass and yield (EC values recalculated based on reported data) NOEC (72h): <5 µg/L element (estimated) based on: biomass and yield (EC values recalculated based on reported data)	2 (reliable with restrictions) key study experimental study **Test material** Dihydrogen tetrachloropalladate (II); palladium(4+) tetrachloride / 16970-55-1 / 241-047-9, Form: liquid (full information in **Annex II**). **Reference** **Pawlowski and Wydra 2005**
Chlamydomonas reinhardtii (algae) freshwater toxicity to aquatic algae and cyanobacteria equivalent or similar to OECD Guideline 201 (Alga, Growth Inhibition Test) [before 23 March 2006]	EC50 (96h): 5.7 µg/L element (meas. (geom. mean)) based on: cell number EC10 (96h): 4.48 µg/L element (meas. (geom. mean)) based on: cell number (EC10 re-calculated using Graph & TRAP software; 95% CI: 4.1-4.9) EC50 (24h): 10.1 µg/L element (meas. (geom. mean)) based on: cell number (value as reported in publication) EC50 (48h): 8.7 µg/L element (meas. (geom. mean)) based on: cell number (value as reported in publication) EC50 (72h): 6.5 µg/L element (meas. (geom. mean)) based on: cell number EC10 (72h): 5.06 µg/L element (meas. (geom. mean)) based on: cell number (EC10 re-calculated using Graph & TRAP software; 95% CI: 4.5-5.8)	2 (reliable with restrictions) key study experimental study **Test material** Palladium dichloride dihydrate; palladium(2+) dichloride / 7647-10-1 / 231-596-2, Form: not specified (full information in **Annex II**). **Reference** **Roy G 2009**
Chlamydomonas reinhardtii (algae) freshwater toxicity to aquatic algae and cyanobacteria equivalent or similar to OECD Guideline 201 (Alga, Growth Inhibition Test) [before 23 March 2006]	EC50 (24h): 7 µg/L element (meas. (geom. mean)) based on: cell number (pH7.0) EC10 (24h): 3.05 µg/L element (meas. (geom. mean)) based on: cell number (EC10 re-calculated using Graph & TRAP software; 95%CI: 1.6-5.9; pH7) EC50 (24h): 10 µg/L element (meas. (geom. mean)) based on: cell number (pH6.0) EC50 (96h): >=30 µg/L element (nominal) based on: cell number (pH8 - no effect observed at 24, 48, 72 and 96h) EC10 (24h): 5.2 µg/L element (meas. (geom. mean)) based on: cell number (EC10 re-calculated using Graph & TRAP software; 95%CI: 4.8-5.6; pH6)	2 (reliable with restrictions) key study experimental study **Test material** Palladium dichloride dihydrate; palladium(2+) dichloride / 7647-10-1 / 231-596-2, Form: not specified (full information in **Annex II**).

		Reference **Tetrault G 2014**
Desmodesmus subspicatus (previous name: Scenedesmus subspicatus) (algae) freshwater toxicity to aquatic algae and cyanobacteria according to OECD Guideline 201 (Alga, Growth Inhibition Test) [before 23 March 2006]	EC50 (72h): 8 µg/L element (meas. (not specified)) based on: biomass (EC50 value recalculated using TRAP based on reported data - 95% CI 7-9) EC10 (72h): 5.3 µg/L element (meas. (not specified)) based on: biomass (EC10 value recalculated using TRAP based on reported data - 95%CI 4-7 µg Pd/L) EC50 (72h): 0.066 mg/L test mat. (nominal) based on: biomass EC50 (24h): 0.078 mg/L test mat. (nominal) based on: growth rate (Extrapolated value) NOEC (72h): 0.04 mg/L test mat. (nominal) based on: growth rate	2 (reliable with restrictions) key study experimental study **Test material** 134620-00-1 / 134620-00-1; Tetrammine Palladium Hydrogen Carbonate, (full information in **Annex II**). **Reference** **Mead C 1997**
Pseudokirchneriella subcapitata (previous names: Raphidocelis subcapitata, Selenastrum capricornutum) (algae) freshwater toxicity to aquatic algae and cyanobacteria according to OECD Guideline 201 (Alga, Growth Inhibition Test) [before 23 March 2006]	EC50 (72h): 4.3 µg/L element (meas. (geom. mean)) based on: growth rate EC10 (72h): 2.7 µg/L element (meas. (geom. mean)) based on: growth rate 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)	1 (reliable without restriction) key study experimental study **Test material** Tetraamminepalladium (II) chloride, Form: not specified (full information in **Annex II**). **Reference** **Wenzel A 2018**

7.1.4. Sediment organisms

The results are summarised in the following table:

Table 7.5. Effects on sediment organisms

Method	Results	Remarks
Chironomus riparius freshwater sediment toxicity: long-term (laboratory study) static Sediment: artificial sediment according to OECD Guideline 218 (Sediment-Water Chironomid Toxicity Test Using Spiked Sediment)	NOEC (28d): >=27.4 mg/kg sediment dw element - Palladium (meas. (arithm. mean)) based on: emergence rate - development rate and development time NOEC (28d): >=54.3 mg/kg sediment dw test mat. - DDP (meas. (arithm. mean)) based on: emergence rate - development rate and development time EC10 (28d): >54.3 mg/kg sediment dw test mat. - DDP (meas. (arithm. mean)) based	1 (reliable without restriction) key study experimental study **Test material** 14323-43-4 / 238-269-3; Diamminedichloropalladium (II),

	on: emergence rate - development rate and development time (95% CL: not determined) EC10 (28d): >27.4 mg/kg sediment dw element - Palladium (meas. (arithm. mean)) based on: emergence rate - development rate and development time (95% CL: not determined) EC50 (28d): >54.3 mg/kg sediment dw test mat. - DDP (meas. (arithm. mean)) based on: emergence rate - development rate and development time (95% CL: not determined) EC50 (28d): >27.4 mg/kg sediment dw element - Palladium (meas. (arithm. mean)) based on: emergence rate - development rate and development time (95% CL: not determined)	Form: solid: particulate/powder - migrated information: powder (full information in **Annex II**). **Reference** **Simon 2013**

7.1.5. Other aquatic organisms

No relevant information available.

7.2. Terrestrial compartment

7.2.1. Toxicity to soil macro-organisms

The results are summarised in the following table:

Table 7.6. Effects on soil macro-organisms

Method	Results	Remarks
Folsomia candida [Collembola (soil-dwelling springtail)] (Collembola (soil-dwelling springtail)) Application method: soil toxicity to terrestrial arthropods: long-term (laboratory study) according to OECD Guideline 232 (Collembolan Reproduction Test in Soil)	NOEC - determined as LOEC/2 (effect at first dose is 19%) (28d): 2.5 µmol/L test mat. (nominal) based on: reproduction (- corresponds to 0.05 mg Pd/kg (dry soil)) EC10 - self-calculated from data (28d): 71.3 mg/kg soil dw element (nominal) based on: reproduction EC50 (28d): 21 µmol/L test mat. (nominal) based on: reproduction (corresponding to 0.43 mg Pd/kg(dw)) EC50 - self calculated from data (28d): 584 mg/kg soil dw element (nominal) based on: reproduction	3 (not reliable) supporting study experimental study **Test material** palladium(2+) dichloride / 7647-10-1 / 231-596-2, Form: solid (full information in **Annex II**). **Reference** **Nemcova B. et al. 2013**
Enchytraeus crypticus (Soil dwelling worm) Application method: soil toxicity to terrestrial arthropods: long-term (laboratory study) according to ISO 16387, OECD 220	NOEC - determined as LOEC/2 (effect at first dose 12%) (28d): 2.5 µmol/l test mat. (nominal) based on: mortality (corresponds to 0.05 mg Pd/kg(dwt)) EC10 - self-calculated from data (28d): 102 mg/kg soil dw element (nominal) based on: reproduction	3 (not reliable) supporting study experimental study **Test material** palladium(2+) dichloride / 7647-10-

	EC50 (28d): 70 µmol/L test mat. (nominal) based on: reproduction (corresponds to 1.42 mg Pd/kg(dry soil)) EC50 - self calculated from data (28d): 1947 mg/kg soil dw element (nominal) based on: reproduction	1 / 231-596-2, Form: solution (full information in **Annex II**). **Reference** **Havelkova. B et al. 2014**

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

The results are summarised in the following table:

Table 7.7. Effects on terrestrial arthropods

Method	Results	Remarks

7.3. Atmospheric compartment

No relevant information available.

7.4. Microbiological activity in sewage treatment systems

The results are summarised in the following table:

Table 7.8. Effects on micro-organisms

Method	Results	Remarks
activated sludge of a predominantly domestic sewage freshwater static according to OECD Guideline 209 (Activated Sludge, Respiration Inhibition Test [before 22 July 2010] ; according to EU Method C.11 (Biodegradation: Activated Sludge Respiration Inhibition Test)	EC10 (3h): 14590 µg/L element (nominal) based on: inhibition of total respiration - respiration rate NOEC (3h): 18 mg/L test mat. - Diamminedichloropalladium (nominal) based on: inhibition of total respiration - respiration rate EC10 (3h): 29 mg/L test mat. - Diamminedichloropalladium (nominal) based on: inhibition of total respiration - respiration rate (95% CL 28 - 30 mg/L) EC50 (3h): 61 mg/L test mat. - Diamminedichloropalladium (nominal) based on: inhibition of total respiration - respiration rate (95% CL 59 - 63 mg/L)	1 (reliable without restriction) key study experimental study **Test material** 14323-43-4 / 238-269-3, Form: solid: particulate/powder - migrated information: powder (full information in **Annex II**). **Reference** **Muckle 2012**
activated sludge of a predominantly	EC10 (3h): 5260 µg/L element (nominal)	2 (reliable with

domestic sewage freshwater static according to OECD Guideline 209 (Activated Sludge, Respiration Inhibition Test [before 22 July 2010]	based on: inhibition of total respiration - respiration rate EC50 (30min): >100 mg/L test mat. (nominal) based on: inhibition of total respiration - respiration rate EC50 (3h): 35 mg/L test mat. (nominal) based on: inhibition of total respiration - respiration rate	restrictions) key study experimental study **Test material** 134620-00-1 / 134620-00-1; Tetrammine Palladium Hydrogen Carbonate, (full information in **Annex II**). **Reference** **Mead C, Worth M 1995**
activated sludge of a predominantly domestic sewage freshwater - deionized water, free from inhibitory concentrations of toxic substances (e.g. Cu2+ ions) + synthetic sewage was used. static according to OECD Guideline 209 (Activated Sludge, Respiration Inhibition Test [before 22 July 2010] ; according to EU Method C.11 (Biodegradation: Activated Sludge Respiration Inhibition Test)	EC10 (3h): 6900 µg/L element (nominal) based on: inhibition of total respiration - Inhibition based on total microbial respiration rate of the activated sludge NOEC (3h): 15.87 mg/L test mat. (nominal) based on: inhibition of total respiration - Inhibition based on total microbial respiration rate of the activated sludge EC10 (3h): 16.42 mg/L test mat. (nominal) based on: inhibition of total respiration - Inhibition based on total microbial respiration rate of the activated sludge (95% Confidence Interval 11.18-20.73 mg/L) EC50 (3h): 44.64 mg/L test mat. (nominal) based on: inhibition of total respiration - Inhibition based on total microbial respiration rate of the activated sludge (95% Confidence Interval 39.04-51.60 mg/L) EC20 (3h): 23.14 mg/L test mat. (nominal) based on: inhibition of total respiration - Inhibition based on total microbial respiration rate of the activated sludge (95% Confidence Interval 17.66-27.56 mg/L)	1 (reliable without restriction) key study experimental study **Test material** Tetraamminepalladium (II) chloride, Form: not specified (full information in **Annex II**). **Reference** **Simon M 2019**

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 7.9. Hazard assessment conclusion for the environment

Compartment	Hazard conclusion	Remarks/Justification
Freshwater	PNEC aqua (freshwater): 0.045µg/L Intermittent releases:	Assessment factor: 50 Extrapolation method: assessment factor PNEC aqua (freshwater) cfr. PNEC derivation report (IUCLID Section 13)
Marine water	PNEC aqua (marine water): 0.004µg/L Intermittent releases:	Assessment factor: 500 Extrapolation method: assessment factor PNEC aqua (marine water) cfr. PNEC derivation report (IUCLID Section 13)
Sediments (freshwater)	PNEC sediment (freshwater): 0.274mg/kg sediment dw	Assessment factor: 100 Extrapolation method: assessment factor PNEC sediment (freshwater) cfr. PNEC derivation report (IUCLID Section 13)
Sediments (marine water)	PNEC sediment (marine water): 0.027mg/kg sediment dw	Assessment factor: 1000 Extrapolation method: assessment factor PNEC sediment (marine water) cfr. PNEC derivation report (IUCLID Section 13)
Sewage treatment plant	PNEC STP: 526µg/L	Assessment factor: 10 Extrapolation method: assessment factor PNEC STP cfr. PNEC derivation report (IUCLID Section 13)
Soil	PNEC soil: 0.02mg/kg soil dw	Extrapolation method: equilibrium partitioning method PNEC soil cfr. PNEC derivation report (IUCLID Section 13)
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 soluble metal substances under consideration is based on the lowest acute and chronic threshold values from the Pd ecotoxicity test data:

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

-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 µg Pd/L; Wenzel 2018)).

The derivation of both ERV values is detailed in the read-across justification report (cfr. IUCLID Section 13) 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). This results in a classification as Acute Category 1 and Chronic Category 1 for all substances contained in the below table. Acute and chronic M-factors are based on the value of the substance-specific acute and chronic ERV, as outlined in ECHA Guidance on the application of the CLP criteria (version 5.0; ECHA, 2017) - cfr. below table.

Substance name	Molecular formula	MWt	Pd Wt%	Acute ERV (µg TI/L)	Chronic ERV (µg TI/L)	Acute aquatic hazard	Acute M-factor	Long-term aquatic hazard	Chronic M-factor
Palladium dichloride	PdCl2	177.3	60.0	5.9	3.8	category Acute 1	M=100	category Chronic 1	M=10
Dihydrogen tetrachloropalladate	Cl4Pd.2H	250.2	42.5	8.4	5.3	category Acute 1	M=100	category Chronic 1	M=10
Palladium sulphate	PdSO4	202.5	52.6	6.8	4.3	category Acute 1	M=100	category Chronic 1	M=10
Disodium tetrachloropalladate	Na2PdCl4	294.2	36.2	9.9	6.2	category Acute 1	M=100	category Chronic 1	M=10
Diamminedichloropalladium	Cl2H6N2Pd	211.4	50.3	7.1	4.5	category Acute 1	M=100	category Chronic 1	M=10
Tetraamminepalladium (II) nitrate	H12N4Pd(NO3)2	298.6	35.6	10.0	6.3	category Acute 1	M=10	category Chronic 1	M=10
Tetraamminepalla	H8Cl2N4Pd	241.4	44.1	8.1	5.1	category Acute 1	M=100	category Chronic 1	M=10

dium(2+) dichloride									
Tetraamminepalladium(2+) dihydroxide	H12N4Pd(OH)2	208.6	51.0	7.0	4.4	category Acute 1	M=100	category Chronic 1	M=10
Tetrammi nepalladium(2+) diacetate	C4H22N4O6Pd	328.7	32.4	11.0	7.0	category Acute 1	M=10	category Chronic 1	M=10
Dipotassium hexachloropalladate	K2PdCl6	397.3	26.8	13.3	8.4	category Acute 1	M=10	category Chronic 1	M=10
Diammonium hexachloropalladate	(NH4)2PdCl6	355.2	30.0	11.9	7.5	category Acute 1	M=10	category Chronic 1	M=10
Tetraamminepalladium(2+) hydrogen carbonate	C2H14O6.N4Pd	296.6	35.9	9.9	6.3	category Acute 1	M=100	category Chronic 1	M=10
Pd acetate	Pd.(C2H3O2)2	224.5	47	7.5	4.8	category Acute 1	M=100	category Chronic 1	M=10

General discussion

This substance is a member of the category of “Palladium & inorganic Palladium substances“. As such,

the data requirements for this substance are covered by relevant and reliable experimental test data generated for all members of this category via a read-across approach.

A read-across justification report and PNEC derivation report are attached in IUCLID Annex 13.

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

Assessment entity linked:
tetraamminepalladium(2+) diacetate. View the assessment entity table in chapter 1.3 **here**;
Pd dissolved. View the assessment entity table in chapter 1.3 **here**

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

As described in section 1 of the CSR several sets of substance properties are needed for the human health and environmental assessment. Therefore assessment entities (AEs) have been defined (see section 1.3), for which relevant properties have been reported in section 1 to 7.
Each contributing scenario has been assessed using the properties of one or more assessment entities, grouped into "assessment entity groups". The defined assessment entity groups are reported in the following table.

Table 9.1. Assessment entity groups

Assessment entity group (AEG) name	Composition of AEG	Remarks
tetraamminepalladium(2+) diacetate for OCC assessment	• 100% tetraamminepalladium(2+) diacetate	**Relevant for the assessment of contributing scenarios for:** - Workers/Consumers **Method for calculating the RCR across the AEs:** Summed RCR
Pd dissolved for ENV assessment	• 100% Pd dissolved	**Relevant for the assessment of contributing scenarios for:** - Environment and Man via environment **Method for calculating the RCR across the AEs:** Summed RCR

9.0.3. Introduction to the assessment for the environment

9.0.3.1. Tonnage

Assessed tonnage: 28 tonnes/year based on:
- 28 tonnes/year manufactured

Tonnage supplied per market sector:

Manufacture of other substances: 28 tonnes/year
The following table provides the tonnage per use and the local tonnages used in the assessment for each environmental contributing activity. The local tonnage corresponds to a tonnage at the site for uses taking place at industrial sites and to a tonnage assumed for a town of 10 000 inhabitants for widespread uses.

Table 9.2. Tonnage for assessment

ES#	Exposure scenario (ES) name and related environmental contributing scenarios	Tonnage per use (t/year)	Daily local tonnage (t/day)	Annual local tonnage (t/year)
ES1 (M)	Manufacture of the substance (as such)	28		
	- Manufacture of the substance (as such) ES 1.1 (ERC 1)		0.1	28
	- Manufacture of the substance (as such) ES 1.2 (ERC 1)		0.1	28
	- Manufacture of the substance (as such) ES 1.3		1.8E-3	0.5

ES#	Exposure scenario (ES) name and related environmental contributing scenarios	Tonnage per use (t/year)	Daily local tonnage (t/day)	Annual local tonnage (t/year)
	(ERC 1)			
ES2 (IS)	Use as an intermediate	28		
	- Use as an intermediate ES 2.1 (ERC 6a)		0.1	28
	- Use as an intermediate ES 2.2 (ERC 6a)		0.1	28
	- Use as an intermediate ES 2.3 (ERC 6a)		1.8E-3	0.5

9.0.3.2. Scope and type of assessment for the environment

The scope of exposure assessment and type of risk characterisation required for the environment are described in the following table based on the hazard conclusions presented in section 7.

Table 9.3. Type of risk characterisation required for the environment

Protection target	Assessment entity	Risk characterisation type	Hazard conclusion (see section 7)
Fresh water	Pd dissolved	Quantitative	PNEC aqua (freshwater) = 0.045 µg/L
Sediment (freshwater)	Pd dissolved	Quantitative	PNEC sediment (freshwater) = 0.274 mg/kg sediment dw
Marine water	Pd dissolved	Quantitative	PNEC aqua (marine water) = 4.5E-3 µg/L
Sediment (marine water)	Pd dissolved	Quantitative	PNEC sediment (marine water) = 0.027 mg/kg sediment dw
Sewage Treatment Plant	Pd dissolved	Quantitative	PNEC STP = 526 µg/L
Air	Pd dissolved	Not needed	No hazard identified
Agricultural soil	Pd dissolved	Quantitative	PNEC soil = 0.02 mg/kg soil dw
Predator’s prey (freshwater)	Pd dissolved	Not needed	No potential for bioaccumulation
Predator’s prey (marine water)	Pd dissolved	Not needed	No potential for bioaccumulation
Top predator’s prey (marine water)	Pd dissolved	Not needed	No potential for bioaccumulation
Predator’s prey (terrestrial)	Pd dissolved	Not needed	No potential for bioaccumulation

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 9.4. Substance key phys-chem and fate properties

Substance property	Pd dissolved
Molecular weight	≥ 106.4
Molecular weight used for the assessment	106.4
Vapour pressure	2.39E-3 Pa at 25 °C

Substance property	Pd dissolved
Water solubility	1.01E3 g/L at 20 °C
Log Kp (solids-water in soil)	2.64 at 25 °C
Log Kp (solids water in sediment)	3.39 at 23 °C
Log Kp (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:

Assessment entities	Pd dissolved
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 for some assessment entities.
Explanation for Pd dissolved:
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 (Clocal) and the regional concentrations (PEC regional).
Fourteen sites involved in the production and processing of Pd substances submitted local emission and exposure information for locations in Germany, Switzerland, Norway, Belgium the Netherlands, Italy and UK. These sites produce and process a number of different Pd compounds and it is important to note that the environment emissions cannot be allocated to a specific substance, activity or process because they are generally collected to a central treatment plant and discharged as a single discharge (e.g. emissions from wastewater treatment plant, WWTP). As a consequence, the environmental exposure estimates relate to Pd originating from the production/use of Pd metal as well as multiple Pd compounds. A sector approach rather than a substance approach is therefore taken to environmental exposure assessment for Pd.
Monitoring data from the Pd processing sector were applied where available (i.e. for manufacturers) or refinements were made to the release factors detailed by SpERCs on the basis of the monetary value of Pd compounds. The use of site-specific monitoring data and representative emission values resulted in RCR values of <1 for all environmental compartments for the manufacturers who also use Pd compounds as intermediates at the same sites. In the absence of site-specific or representative emission data for downstream users the release factors (RFs) detailed in the SpERCs were adjusted based on the monetary value of Pd compounds. The RFs in SpERCs are generally based on measured emissions from sites producing or using base metals such as nickel, tin and zinc. Due to the considerably higher monetary value of Pd it is considered that emissions from the manufacture and use of palladium substances are likely to be at least an order of magnitude lower and release factors for water and air from the SpERCs have been adjusted accordingly. This is supported by the available measured data for manufacture and use as intermediates at industrial sites, i.e. the release factors to water and air for manufacture and intermediate use of palladium compounds based on sector data (56 and 22 g/T, respectively) are 13 to 36 times lower than the relevant SpERC-defined release factors (2,000 and 300 g/T for water and air, respectively). An order of magnitude reduction in release estimate is therefore considered to be a reasonably conservative default and emissions to water and air based on RFs taken from the SpERC documents have been adjusted to 10% of the recommended value.

Summary information gathered from the Pd industry:

Value	Site Tonnage (tpa Pd, 2012-15)	Emission days per site (d/yr)	
		Water	Air
Median (50P)	9.5	280	330

Value	Site Tonnage (tpa Pd, 2012-15)	Emission days per site (d/yr)	
		Water	Air
90th % Percentile (90P)	28.0	365	365
Min	-	50	250
Max	-	365	365
n	14	13	13
Selected for Exposure Scenario	28.0 (90P)	280 (50P)	330(50P)

Value	Release factor (RF) (g/T)	On-site effluent flow (m^3/d)	STP flow (m^3/d)	River flow rate (m^3/d)	Dilution factor to STP	Dilution factor STP to river
Median (50P)	56.2	120	25000	6972480	334	32
90P	424	400	177586.5	16000000	13960	641
10P	1.5	3.6	2995	51083.4	22.7	4.31
Min	0.2	1	2950	2950	15	2
Max	833	2592	1344000	16000000	25000	641
N	12	13	10	8	9	7
Selected for ES 1.1 & 2.1 Freshwater – via STP	56.2 (50P)	120 (50P)	3000 (10P STP flow rate)		25 (based on median effluent flow rate & 10P STP flow)	32 (median dilution factor)
Selected for ES 1.2 & 2.2 Freshwater – direct discharge to water		3000		1000 max (dilution factor for only site with direct discharge is 4800)		
Selected for ES 1.3 & 2.3 Marine		On-site: 120 (50P)				100 (default)

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 9.5. Type of risk characterisation required for workers

Route	Type of effect	Assessment entity	Risk characterisation type	Hazard conclusion (see section 5.11)
Inhalation	Systemic effects - long term	tetraamminepalladium(2+) diacetate	Quantitative	DNEL (Derived No Effect Level) = 0.26 mg/m³
	Systemic effects - acute	tetraamminepalladium(2+) diacetate	Not needed	No hazard identified
	Local effects - long term	tetraamminepalladium(2+) diacetate	Qualitative	Medium hazard (no threshold derived)
	Local effects - acute	tetraamminepalladium(2+) diacetate	Qualitative	Medium hazard (no threshold derived)
Dermal	Systemic effects - long term	tetraamminepalladium(2+) diacetate	Quantitative	DNEL (Derived No Effect Level) = 0.36 mg/kg bw/day
	Systemic effects - acute	tetraamminepalladium(2+) diacetate	Not needed	No hazard identified
	Local effects - long term	tetraamminepalladium(2+) diacetate	Qualitative	High hazard (no threshold derived)
	Local effects - acute	tetraamminepalladium(2+) diacetate	Qualitative	High hazard (no threshold derived)
Eye	Local effects	tetraamminepalladium(2+) diacetate	Qualitative	Low 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). QUALITATIVE RISK CHARACTERISATION FOR LOCAL EFFECTS In addition to the quantitative risk characterisation, demonstrating that prescribed operational conditions and risk management measures effectively control exposure well below the respective DNELs, residual exposure concentrations may theoretically still cause local effects. As a precautionary measure, it is therefore prescribed to use personal protective equipment in situations in which such residual exposure concentrations cannot be excluded. The risk of local effects is therefore adequately controlled. Please refer to the document “Methodology applied in the occupational exposure scenarios for palladium substances” as annexed to the CSR for further information on the applied methodology for the occupational exposure assessment.

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. DERMAL ROUTE (SKIN PROTECTION) When dermal protective equipment is required, specific information is provided in the occupational exposure scenarios below. Further, dermal 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. Certified safety clothing including coveralls and safety shoes are generally worn. Protective gloves comply with EN 374 and are

changed according to manufacturer’s information or when damaged, whatever is the earlier. INHALATION ROUTE (RESPIRATORY PROTECTION) When respiratory protective equipment (RPE) is required, specific information on the required assigned protection factor (APF) is provided in the occupational exposure scenarios below. RPE should be selected based on the given APF according to EN 529 and should comply with national legislation. If RPE has to be worn, an APF of 10 represents the required minimum level of protection. RPE shall only be worn if the following principles are implemented in parallel: The duration of work should take into account the additional physiological stress for the worker due to the breathing resistance and mass of the RPE itself and due to the increased thermal stress by enclosing the head. In addition, it shall be considered that the worker’s capability of using tools and of communicating are reduced during the wearing of RPE. For reasons as given above, the worker should therefore: (i) be healthy (especially in view of medical problems that may affect the use of RPE), and (ii) have suitable facial characteristics reducing leakages between face and mask (in view of scars and facial hair). The devices recommended in the ES which rely on a tight face seal will not provide the required protection unless they fit the contours of the face properly and securely. The employer and self-employed persons have legal responsibilities for the maintenance and supply of respiratory protective devices and the management of their correct use in the workplace. Therefore, they should define and document a suitable policy for a respiratory protective device programme including training of workers. 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) ES 1.1	ERC 1
CS 2	Manufacture of the substance (as such) ES 1.2	ERC 1
CS 3	Manufacture of the substance (as such) ES 1.3	ERC 1
Worker contributing scenario(s):		
CS 4	Fully contained processes	PROC 1
CS 5	Handling/Transfer of solutions	PROC 8b
CS 6	Wet cleaning	PROC 8a

Further description of the use:

Tetraammine palladium (2+) diacetate is manufactured by adding an inorganic Pd precursor to an ammine ligand and an acetate source.

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) ES 1.1 (ERC 1)

Assessment entity group used for the assessment of this contributing scenario: Pd dissolved for ENV assessment

9.1.1.1. Conditions of use

Amount used, frequency and duration of use (or from service life)
• Annual use amount at site: <= 28 tonnes/year *86.5 tonnes tetraamminepalladium (2+) diacetate (28.0 tonnes Pd metal equivalent); 90P from sector data*
• Daily use amount at site: <= 0.1 tonnes/day *Based on 280 days per year (50P from sector data)*
Conditions and measures related to biological sewage treatment plant
• Biological STP: Site specific [Effectiveness Water: 73.4%]
• Discharge rate of STP: >= 3E3 m3/day
• Application of the STP sludge on agricultural soil: No *The sludge is incinerated (with ash going to landfill)*
Conditions and measures related to external treatment of waste (including article waste)
• Particular considerations on the waste treatment operations: Other *Dihydrogen tetrachloropalladate- and other Pd -containing waste suitable for recycling may be recycled either internally or at licensed recycling facility.* *The sludge from the on-site treatment plant is processed for metal reclamation (recycling).*
Other conditions affecting environmental exposure
• Receiving surface water flow rate: >= 9.3E4 m3/day *based on 50P dilution factor from sector data*
• Discharge to: Freshwater only

Fate (release percentage) in the biological sewage treatment plant

The biological STP is site specific and the releases to the various compartments have been set by the assessor for some assessment entities. They are distributed in the following way:

Assessment entities	**Pd dissolved**
Release to water	26.6%

Assessment entities	Pd dissolved
Release to air	0%
Release to sludge	73.4%
Release degraded	0%

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

9.1.1.2. Releases

The local releases to the environment are reported in the following table. Note that the releases reported do not account for the removal in the modelled biological STP.

Table 9.6. Local releases to the environment

Release	Assessment entity	Release estimation method	Explanations
Water	Pd dissolved	Estimated release factor	**Release factor before on site RMM:** 5.62E-3% **Release factor after on site RMM:** 5.62E-3% **Local release rate:** 5.62E-3 kg/day **Explanation:** On-site wastewater treatment by chemical precipitation, sedimentation and/or filtration. Efficiency 99.9 % (sector data) Release factor after on-site treatment: 56.2 g/T (50P from sector data)
Air	Pd dissolved	Estimated release factor	**Release factor before on site RMM:** 3E-3% **Release factor after on site RMM:** 3E-3% **Local release rate:** 3E-3 kg/day **Explanation:** Treatment of air emissions by wet scrubbers and filters (e.g. fabric, bag, HEPA). Release factor after on-site treatment: 30 g/T (10% of SpERC RF for 'Manufacture of metal compounds')
Non agricultural soil	Pd dissolved	Estimated release factor	**Release factor after on site RMM:** 0% **Explanation:** No direct emissions to soil.

9.1.1.3. Exposure and risks for the environment and man via the environment

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table. The exposure estimates have been obtained with EUSES 2.1.2 unless stated otherwise.

Table 9.7. Exposure concentrations and risks for the environment and man via the environment

Protection target	Assessment entity	Exposure concentration	Risk quantification
Fresh water	Pd dissolved	**Local PEC:** 1.52E-5 mg/L RCR = 0.338	Final RCR = 0.338
Sediment (freshwater)	Pd dissolved	**Local PEC:** 0.037 mg/kg dw RCR = 0.136	Final RCR = 0.136
Sewage Treatment Plant	Pd dissolved	**Local PEC:** 4.98E-4 mg/L RCR = 9.47E-4	Final RCR < 0.01
Agricultural soil	Pd dissolved	**Local PEC:** 1.89E-3 mg/kg dw RCR = 0.096	Final RCR = 0.096

9.1.2. Env CS 2: Manufacture of the substance (as such) ES 1.2 (ERC 1)

Assessment entity group used for the assessment of this contributing scenario: Pd dissolved for ENV assessment

9.1.2.1. Conditions of use

Amount used, frequency and duration of use (or from service life)
• Annual use amount at site: <= 28 tonnes/year *86.5 tonnes tetraamminepalladium (2+) diacetate (28.0 tonnes Pd metal equivalent); 90P from sector data*
• Daily use amount at site: <= 0.1 tonnes/day *Based on 280 days per year (50P from sector data)*
Conditions and measures related to biological sewage treatment plant
• Biological STP: None [Effectiveness Water: 0%]
Conditions and measures related to external treatment of waste (including article waste)
• Particular considerations on the waste treatment operations: Other *Dihydrogen tetrachloropalladate- and other Pd -containing waste suitable for recycling may be recycled either internally or at licensed recycling facility.* *The sludge from the on-site treatment plant is processed for metal reclamation (recycling).*
Other conditions affecting environmental exposure
• Discharge to: Freshwater only
• Discharge rate of effluent: >= 3E3 m3/day
• Receiving surface water flow rate: >= 2.98E6 m3/day

9.1.2.2. Releases

The local releases to the environment are reported in the following table. Note that the releases reported do not account for the removal in the modelled biological STP.

Table 9.8. Local releases to the environment

Release	Assessment entity	Release estimation method	Explanations
Water	Pd dissolved	Estimated release factor	**Release factor before on site RMM:** 5.62E-3% **Release factor after on site RMM:** 5.62E-3% **Local release rate:** 5.62E-3 kg/day **Explanation:** On-site wastewater treatment by chemical precipitation, sedimentation and/or filtration. Efficiency 99.9 % (sector data) Release factor after on-site treatment: 56.2 g/T (50P from sector data)
Air	Pd dissolved	Estimated release factor	**Release factor before on site RMM:** 3E-3% **Release factor after on site RMM:** 3E-3% **Local release rate:** 3E-3 kg/day **Explanation:** Treatment of air emissions by wet scrubbers and filters (e.g. fabric, bag, HEPA). Release factor after on-site treatment: 30 g/T (10% of SpERC RF for 'Manufacture of metal compounds')
Non agricultural soil	Pd dissolved	Estimated release factor	**Release factor after on site RMM:** 0% **Explanation:** No direct emissions to soil.

9.1.2.3. Exposure and risks for the environment and man via the environment

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table. The exposure estimates have been obtained with EUSES 2.1.2 unless stated otherwise.

Table 9.9. Exposure concentrations and risks for the environment and man via the environment

Protection target	Assessment entity	Exposure concentration	Risk quantification
Fresh water	Pd dissolved	**Local PEC:** 1.99E-6 mg/L RCR = 0.044	Final RCR = 0.044
Sediment (freshwater)	Pd dissolved	**Local PEC:** 4.9E-3 mg/kg dw RCR = 0.018	Final RCR = 0.018
Agricultural soil	Pd dissolved	**Local PEC:** 1.89E-3 mg/kg dw RCR = 0.096	Final RCR = 0.096

9.1.3. Env CS 3: Manufacture of the substance (as such) ES 1.3 (ERC 1)

Assessment entity group used for the assessment of this contributing scenario: Pd dissolved for ENV assessment

9.1.3.1. Conditions of use

Amount used, frequency and duration of use (or from service life)
• Annual use amount at site: <= 0.5 tonnes/year *1.54 tonnes tetraamminepalladium (2+) diacetate (0.50 tonnes Pd metal equivalent); calculated Msafe*
• Daily use amount at site: <= 1.8E-3 tonnes/day *Based on 280 days per year (50P from sector data)*
Conditions and measures related to biological sewage treatment plant
• Biological STP: None [Effectiveness Water: 0%]
Conditions and measures related to external treatment of waste (including article waste)
• Particular considerations on the waste treatment operations: Other *Dihydrogen tetrachloropalladate- and other Pd -containing waste suitable for recycling may be recycled either internally or at licensed recycling facility.* *The sludge from the on-site treatment plant is processed for metal reclamation (recycling).*
Other conditions affecting environmental exposure
• Discharge to: Marine water only
• Dilution factor to marine water: <= 100
• Discharge rate of effluent: >= 120 m3/day

9.1.3.2. Releases

The local releases to the environment are reported in the following table. Note that the releases reported do not account for the removal in the modelled biological STP.

Table 9.10. Local releases to the environment

Release	Assessment entity	Release estimation method	Explanations
Water	Pd dissolved	Estimated release factor	**Release factor before on site RMM:** 1E-3% **Release factor after on site RMM:** 1E-3% **Local release rate:** 1.8E-5 kg/day **Explanation:** Arbitrary
Air	Pd dissolved	Estimated release factor	**Release factor before on site RMM:** 3E-3% **Release factor after on site RMM:** 3E-3% **Local release rate:** 5.4E-5 kg/day **Explanation:** Treatment of air emissions by wet scrubbers and filters (e.g. fabric, bag, HEPA). Release factor after on-site treatment: 30 g/T (10% of SpERC RF for ‘Manufacture of metal compounds’)

Release	Assessment entity	Release estimation method	Explanations
Non agricultural soil	Pd dissolved	Estimated release factor	**Release factor after on site RMM:** 0% **Explanation:** No direct emissions to soil.

9.1.3.3. Exposure and risks for the environment and man via the environment

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table. The exposure estimates have been obtained with EUSES 2.1.2 unless stated otherwise.

Table 9.11. Exposure concentrations and risks for the environment and man via the environment

Protection target	Assessment entity	Exposure concentration	Risk quantification
Marine water	Pd dissolved	Clocal: 1.2E-6 mg/L (estimated by Calculation with Kp susp. matter marine (logKp = 4.21)) RCR = 0.27	Final RCR = 0.27
Sediment (marine water)	Pd dissolved	Clocal: 0.02 mg/kg dw (estimated by Calculation with Kp susp. matter marine (logKp = 4.21)) RCR = 0.735	Final RCR = 0.735
Agricultural soil	Pd dissolved	**Local PEC:** 1.85E-3 mg/kg dw RCR = 0.094	Final RCR = 0.094

9.1.4. Worker CS 4: Fully contained processes (PROC 1)

Assessment entity group used for the assessment of this contributing scenario: tetraamminepalladium(2+) diacetate for OCC assessment

9.1.4.1. Conditions of use

	Method
Product (article) characteristics	
• Content in preparation: Not restricted [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
• Maximum emission potential of the substance: Very low	MEASE 1
• Physical form of substance: Solution	MEASE 1
Amount used (or contained in articles), frequency and duration of use/exposure	
• Maximum duration of exposure: > 240 min (not restricted) [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
Technical and organisational conditions and measures	
• Contact level: None	MEASE 1
• Level of containment: Closed process	MEASE 1
• Pattern of exposure control: Non-direct handling	MEASE 1
• Pattern of use: Closed system without breaches	MEASE 1
• Maximum process temperature: 100 °C	MEASE 1
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protective equipment (RPE) as precautionary measure: RPE protecting from local effects via inhalation	
• Gloves as precautionary measure: Gloves protecting from local effects to the skin (high hazard)	
• Eye protection: Eye protection to be worn to protect from adverse effects to the eyes	

9.1.4.2. Exposure and risks for workers

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table.

Table 9.12. Exposure concentrations and risks for workers

Route of exposure and type of effects	Assessment entity	Exposure concentration	Risk quantification
Inhalation, systemic, long term	tetraamminepalladium(2+) diacetate	1 µg/m³ (MEASE 1) RCR = 3.85E-3	Final RCR < 0.01
Dermal, systemic, long term	tetraamminepalladium(2+) diacetate	1.71 µg/kg bw/day (MEASE 1) RCR = 4.75E-3	Final RCR < 0.01
Combined routes, systemic, long-term			Final RCR < 0.01

Remarks on exposure data from external estimation tools:

MEASE 1 for tetraamminepalladium(2+) diacetate:
Explanation: Dermal, systemic, long term
For calculation of systemic exposure, the exposure estimate for total dermal loading as obtained in MEASE (reported in mg/day) is divided by a body weight of 70 kg for workers.

Risk characterisation

Qualitative risk characterisation (Inhalation, local, long term, Inhalation, local, acute, Dermal, local, long term, Dermal, local, acute, Eye, local):
Further information on the risk characterisation for local effects via inhalation, for local dermal effects and local effects to the eyes is given in Section 9.0.2.3.
Additional remarks on risk characterisation: Under the prescribed conditions of use, exposure is well below the DNELs and no local effects are expected. Therefore, risks are adequately controlled.

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

Assessment entity group used for the assessment of this contributing scenario: tetraamminepalladium(2+) diacetate for OCC assessment

9.1.5.1. Conditions of use

	Method
Product (article) characteristics	
• Content in preparation: Not restricted [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
• Maximum emission potential of the substance: Very low	MEASE 1
• Physical form of substance: Solution	MEASE 1
Amount used (or contained in articles), frequency and duration of use/exposure	
• Maximum duration of exposure: > 240 min (not restricted) [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
Technical and organisational conditions and measures	
• Contact level: Intermittent	MEASE 1
• Pattern of exposure control: Non-direct handling	MEASE 1
• Pattern of use: Non-dispersive use	MEASE 1
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protective equipment (RPE) as precautionary measure: RPE protecting from local effects via inhalation	
• Gloves as precautionary measure: Gloves protecting from local effects to the skin (high hazard)	
• Eye protection: Eye protection to be worn to protect from adverse effects to the eyes	

9.1.5.2. Exposure and risks for workers

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table.

Table 9.13. Exposure concentrations and risks for workers

Route of exposure and type of effects	Assessment entity	Exposure concentration	Risk quantification
Inhalation, systemic, long term	tetraamminepalladium(2+) diacetate	10 µg/m³ (MEASE 1) RCR = 0.038	Final RCR = 0.038
Dermal, systemic, long term	tetraamminepalladium(2+) diacetate	3.43 µg/kg bw/day (MEASE 1) RCR = 9.53E-3	Final RCR < 0.01
Combined routes, systemic, long-term			Final RCR = 0.048

Remarks on exposure data from external estimation tools:

MEASE 1 for tetraamminepalladium(2+) diacetate:
Explanation: Dermal, systemic, long term
For calculation of systemic exposure, the exposure estimate for total dermal loading as obtained in MEASE (reported in mg/day) is divided by a body weight of 70 kg for workers.

Risk characterisation

Qualitative risk characterisation (Inhalation, local, long term, Inhalation, local, acute, Dermal, local, long term, Dermal, local, acute, Eye, local):
Further information on the risk characterisation for local effects via inhalation, for local dermal effects and local effects to the eyes is given in Section 9.0.2.3.
Additional remarks on risk characterisation: Under the prescribed conditions of use, exposure is well below the DNELs and no local effects are expected. Therefore, risks are adequately controlled.

9.1.6. Worker CS 6: Wet cleaning (PROC 8a)

Assessment entity group used for the assessment of this contributing scenario: tetraamminepalladium(2+) diacetate for OCC assessment

9.1.6.1. Conditions of use

	Method
Product (article) characteristics	
• Content in preparation: Not restricted [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
• Maximum emission potential of the substance: Very low	MEASE 1
• Physical form of substance: Solution	MEASE 1
Amount used (or contained in articles), frequency and duration of use/exposure	
• Maximum duration of exposure: > 240 min (not restricted) [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
Technical and organisational conditions and measures	
• Contact level: Extensive	MEASE 1
• Immediate removal of splashes: Splashes should be removed immediately before drying of the substance	MEASE 1
• Pattern of exposure control: Direct handling	MEASE 1
• Pattern of use: Non-dispersive use	MEASE 1
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protective equipment (RPE) as precautionary measure: RPE protecting from local effects via inhalation	
• Gloves: Protective gloves according to EN 374 have to be worn. Gloves have to be changed according to manufacturer’s information or when damaged, whatever is the	MEASE 1

	Method
earlier. [Effectiveness Dermal: 90%]	
• Eye protection: Eye protection to be worn to protect from adverse effects to the eyes	

9.1.6.2. Exposure and risks for workers

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table.

Table 9.14. Exposure concentrations and risks for workers

Route of exposure and type of effects	Assessment entity	Exposure concentration	Risk quantification
Inhalation, systemic, long term	tetraamminepalladium(2+) diacetate	50 µg/m³ (MEASE 1) RCR = 0.192	Final RCR = 0.192
Dermal, systemic, long term	tetraamminepalladium(2+) diacetate	34.29 µg/kg bw/day (MEASE 1) RCR = 0.095	Final RCR = 0.095
Combined routes, systemic, long-term			Final RCR = 0.288

Remarks on exposure data from external estimation tools:

MEASE 1 for tetraamminepalladium(2+) diacetate:
Explanation: Dermal, systemic, long term
For calculation of systemic exposure, the exposure estimate for total dermal loading as obtained in MEASE (reported in mg/day) is divided by a body weight of 70 kg for workers.

Risk characterisation

Qualitative risk characterisation (Inhalation, local, long term, Inhalation, local, acute, Dermal, local, long term, Dermal, local, acute, Eye, local):
Further information on the risk characterisation for local effects via inhalation, for local dermal effects and local effects to the eyes is given in Section 9.0.2.3.
Additional remarks on risk characterisation: Under the prescribed conditions of use, exposure is well below the DNELs and no local effects are expected. Therefore, risks are adequately controlled.

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

Market sector: Manufacture of other substances
Sector of use: SU 8: Manufacture of bulk, large scale chemicals (including petroleum products); SU 9: Manufacture of fine chemicals

Environment contributing scenario(s):		
CS 1	Use as an intermediate ES 2.1	ERC 6a
CS 2	Use as an intermediate ES 2.2	ERC 6a
CS 3	Use as an intermediate ES 2.3	ERC 6a
Worker contributing scenario(s):		
CS 4	Handling/Transfer of solutions	PROC 8b
CS 5	Small scale handling/transfer of solutions	PROC 9
CS 6	Fully contained reaction process	PROC 1
CS 7	Closed batch reaction process	PROC 3
CS 8	Open or semi-closed wet chemical reaction process	PROC 4
CS 9	Laboratory analyses	PROC 15
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 ES 2.1 (ERC 6a)

Assessment entity group used for the assessment of this contributing scenario: Pd dissolved for ENV assessment

9.2.1.1. Conditions of use

Amount used, frequency and duration of use (or from service life)
• Annual use amount at site: <= 28 tonnes/year *86.5 tonnes tetraamminepalladium (2+) diacetate (28.0 tonnes Pd metal equivalent); 90P from sector data*
• Daily use amount at site: <= 0.1 tonnes/day *Based on 280 days per year (50P from sector data)*
Conditions and measures related to biological sewage treatment plant
• Biological STP: Site specific [Effectiveness Water: 73.4%]
• Discharge rate of STP: >= 3E3 m3/day
• Application of the STP sludge on agricultural soil: No *The sludge is incinerated (with ash going to landfill)*
Conditions and measures related to external treatment of waste (including article waste)
• Particular considerations on the waste treatment operations: Other *Dihydrogen tetrachloropalladate- and other Pd -containing waste suitable for recycling may be recycled either internally or at licensed recycling facility.* *The sludge from the on-site treatment plant is processed for metal reclamation (recycling).*
Other conditions affecting environmental exposure
• Receiving surface water flow rate: >= 9.3E4 m3/day
• Discharge to: Freshwater only

Fate (release percentage) in the biological sewage treatment plant

The biological STP is site specific and the releases to the various compartments have been set by the assessor for some assessment entities. They are distributed in the following way:

Assessment entities	Pd dissolved
Release to water	26.6%
Release to air	0%
Release to sludge	73.4%
Release degraded	0%

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

9.2.1.2. Releases

The local releases to the environment are reported in the following table. Note that the releases reported do not account for the removal in the modelled biological STP.

Table 9.15. Local releases to the environment

Release	Assessment entity	Release estimation method	Explanations
Water	Pd dissolved	Estimated release factor	**Release factor before on site RMM:** 5.62E-3% **Release factor after on site RMM:** 5.62E-3% **Local release rate:** 5.62E-3 kg/day **Explanation:** On-site wastewater treatment by chemical precipitation, sedimentation and/or filtration. Efficiency 99.9 % (sector data) Release factor after on-site treatment: 56.2 g/T (50P from sector data)
Air	Pd dissolved	Estimated release factor	**Release factor before on site RMM:** 3E-3% **Release factor after on site RMM:** 3E-3% **Local release rate:** 3E-3 kg/day **Explanation:** Treatment of air emissions by wet scrubbers and filters (e.g. fabric, bag, HEPA). Release factor after on-site treatment: 30 g/T (10% of SpERC RF for 'Manufacture of metal compounds')
Non agricultural soil	Pd dissolved	Estimated release factor	**Release factor after on site RMM:** 0% **Explanation:** No direct emissions to soil.

9.2.1.3. Exposure and risks for the environment and man via the environment

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table. The exposure estimates have been obtained with EUSES 2.1.2 unless stated otherwise.

Table 9.16. Exposure concentrations and risks for the environment and man via the environment

Protection target	Assessment entity	Exposure concentration	Risk quantification
Fresh water	Pd dissolved	**Local PEC:** 1.52E-5 mg/L RCR = 0.338	Final RCR = 0.338
Sediment (freshwater)	Pd dissolved	**Local PEC:** 0.037 mg/kg dw RCR = 0.136	Final RCR = 0.136
Sewage Treatment Plant	Pd dissolved	**Local PEC:** 4.98E-4 mg/L RCR = 9.47E-4	Final RCR < 0.01

Protection target	Assessment entity	Exposure concentration	Risk quantification
Agricultural soil	Pd dissolved	**Local PEC:** 1.89E-3 mg/kg dw RCR = 0.096	Final RCR = 0.096

9.2.2. Env CS 2: Use as an intermediate ES 2.2 (ERC 6a)

Assessment entity group used for the assessment of this contributing scenario: Pd dissolved for ENV assessment

9.2.2.1. Conditions of use

Amount used, frequency and duration of use (or from service life)
• Annual use amount at site: <= 28 tonnes/year *86.5 tonnes tetraamminepalladium (2+) diacetate (28.0 tonnes Pd metal equivalent); 90P from sector data*
• Daily use amount at site: <= 0.1 tonnes/day *Based on 280 days per year (50P from sector data)*
Conditions and measures related to biological sewage treatment plant
• Biological STP: None [Effectiveness Water: 0%]
Conditions and measures related to external treatment of waste (including article waste)
• Particular considerations on the waste treatment operations: Other *Dihydrogen tetrachloropalladate- and other Pd -containing waste suitable for recycling may be recycled either internally or at licensed recycling facility.* *The sludge from the on-site treatment plant is processed for metal reclamation (recycling).*
Other conditions affecting environmental exposure
• Receiving surface water flow rate: >= 2.98E6 m3/day
• Discharge to: Freshwater only
• Discharge rate of effluent: >= 3E3 m3/day

9.2.2.2. Releases

The local releases to the environment are reported in the following table. Note that the releases reported do not account for the removal in the modelled biological STP.

Table 9.17. Local releases to the environment

Release	Assessment entity	Release estimation method	Explanations
Water	Pd dissolved	Estimated release factor	**Release factor before on site RMM:** 5.62E-3% **Release factor after on site RMM:** 5.62E-3% **Local release rate:** 5.62E-3 kg/day **Explanation:** On-site wastewater treatment by chemical precipitation, sedimentation and/or filtration. Efficiency 99.9 % (sector data) Release factor after on-site treatment: 56.2 g/T (50P from sector data)
Air	Pd dissolved	Estimated release factor	**Release factor before on site RMM:** 3E-3% **Release factor after on site RMM:** 3E-3% **Local release rate:** 3E-3 kg/day **Explanation:** Treatment of air emissions by wet scrubbers and filters (e.g. fabric, bag, HEPA). Release factor after on-site treatment: 30 g/T (10% of SpERC RF for ‘Manufacture of metal compounds’)
Non agricultural soil	Pd dissolved	Estimated release factor	**Release factor after on site RMM:** 0% **Explanation:**

Release	Assessment entity	Release estimation method	Explanations
			No direct emissions to soil.

9.2.2.3. Exposure and risks for the environment and man via the environment

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table. The exposure estimates have been obtained with EUSES 2.1.2 unless stated otherwise.

Table 9.18. Exposure concentrations and risks for the environment and man via the environment

Protection target	Assessment entity	Exposure concentration	Risk quantification
Fresh water	Pd dissolved	**Local PEC:** 1.99E-6 mg/L RCR = 0.044	Final RCR = 0.044
Sediment (freshwater)	Pd dissolved	**Local PEC:** 4.9E-3 mg/kg dw RCR = 0.018	Final RCR = 0.018
Agricultural soil	Pd dissolved	**Local PEC:** 1.89E-3 mg/kg dw RCR = 0.096	Final RCR = 0.096

9.2.3. Env CS 3: Use as an intermediate ES 2.3 (ERC 6a)

Assessment entity group used for the assessment of this contributing scenario: Pd dissolved for ENV assessment

9.2.3.1. Conditions of use

Amount used, frequency and duration of use (or from service life)
• Annual use amount at site: <= 0.5 tonnes/year *1.54 tonnes tetraamminepalladium (2+) diacetate (0.50 tonnes Pd metal equivalent); calculated Msafe*
• Daily use amount at site: <= 1.8E-3 tonnes/day *Based on 280 days per year (50P from sector data)*
Conditions and measures related to biological sewage treatment plant
• Biological STP: None [Effectiveness Water: 0%]
Conditions and measures related to external treatment of waste (including article waste)
• Particular considerations on the waste treatment operations: Other *Dihydrogen tetrachloropalladate- and other Pd -containing waste suitable for recycling may be recycled either internally or at licensed recycling facility.* *The sludge from the on-site treatment plant is processed for metal reclamation (recycling).*
Other conditions affecting environmental exposure
• Discharge to: Marine water only
• Discharge rate of effluent: >= 120 m3/day
• Dilution factor to marine water: <= 100

9.2.3.2. Releases

The local releases to the environment are reported in the following table. Note that the releases reported do not account for the removal in the modelled biological STP.

Table 9.19. Local releases to the environment

Release	Assessment entity	Release estimation method	Explanations
Water	Pd dissolved	Estimated release factor	**Release factor before on site RMM:** 1E-3% **Release factor after on site RMM:** 1E-3% **Local release rate:** 1.8E-5 kg/day

Release	Assessment entity	Release estimation method	Explanations
Air	Pd dissolved	Estimated release factor	**Release factor before on site RMM:** 3E-3% **Release factor after on site RMM:** 3E-3% **Local release rate:** 5.4E-5 kg/day
Non agricultural soil	Pd dissolved	Estimated release factor	**Release factor after on site RMM:** 0%

9.2.3.3. Exposure and risks for the environment and man via the environment

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table. The exposure estimates have been obtained with EUSES 2.1.2 unless stated otherwise.

Table 9.20. Exposure concentrations and risks for the environment and man via the environment

Protection target	Assessment entity	Exposure concentration	Risk quantification
Marine water	Pd dissolved	Clocal: 1.21E-6 mg/L (estimated by Calculation with Kp susp. matter marine (logKp = 4.21)) RCR = 0.273	Final RCR = 0.273
Sediment (marine water)	Pd dissolved	Clocal: 0.02 mg/kg dw (estimated by Calculation with Kp susp. matter marine (logKp = 4.21)) RCR = 0.735	Final RCR = 0.735
Agricultural soil	Pd dissolved	**Local PEC:** 1.85E-3 mg/kg dw RCR = 0.094	Final RCR = 0.094

9.2.4. Worker CS 4: Handling/Transfer of solutions (PROC 8b)

Assessment entity group used for the assessment of this contributing scenario: tetraamminepalladium(2+) diacetate for OCC assessment

9.2.4.1. Conditions of use

	Method
Product (article) characteristics	
• Content in preparation: Not restricted [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
• Maximum emission potential of the substance: Very low	MEASE 1
• Physical form of substance: Solution	MEASE 1
Amount used (or contained in articles), frequency and duration of use/exposure	
• Maximum duration of exposure: > 240 min (not restricted) [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
Technical and organisational conditions and measures	
• Contact level: Intermittent	MEASE 1
• Pattern of exposure control: Non-direct handling	MEASE 1
• Pattern of use: Non-dispersive use	MEASE 1
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protective equipment (RPE) as precautionary measure: RPE protecting from local effects via inhalation	
• Gloves as precautionary measure: Gloves protecting from local effects to the skin (high hazard)	
• Eye protection: Eye protection to be worn to protect from adverse effects to the eyes	

9.2.4.2. Exposure and risks for workers

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table.

Table 9.21. Exposure concentrations and risks for workers

Route of exposure and type of effects	Assessment entity	Exposure concentration	Risk quantification
Inhalation, systemic, long term	tetraamminepalladium(2+) diacetate	10 µg/m³ (MEASE 1) RCR = 0.038	Final RCR = 0.038
Dermal, systemic, long term	tetraamminepalladium(2+) diacetate	3.43 µg/kg bw/day (MEASE 1) RCR = 9.53E-3	Final RCR < 0.01
Combined routes, systemic, long-term			Final RCR = 0.048

Remarks on exposure data from external estimation tools:

MEASE 1 for tetraamminepalladium(2+) diacetate:
Explanation: Dermal, systemic, long term
For calculation of systemic exposure, the exposure estimate for total dermal loading as obtained in MEASE (reported in mg/day) is divided by a body weight of 70 kg for workers.

Risk characterisation

Qualitative risk characterisation (Inhalation, local, long term, Inhalation, local, acute, Dermal, local, long term, Dermal, local, acute, Eye, local):
Further information on the risk characterisation for local effects via inhalation, for local dermal effects and local effects to the eyes is given in Section 9.0.2.3.
Additional remarks on risk characterisation: Under the prescribed conditions of use, exposure is well below the DNELs and no local effects are expected. Therefore, risks are adequately controlled.

9.2.5. Worker CS 5: Small scale handling/transfer of solutions (PROC 9)

Assessment entity group used for the assessment of this contributing scenario: tetraamminepalladium(2+) diacetate for OCC assessment

9.2.5.1. Conditions of use

	Method
Product (article) characteristics	
• Content in preparation: Not restricted [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
• Maximum emission potential of the substance: Very low	MEASE 1
• Physical form of substance: Solution	MEASE 1
Amount used (or contained in articles), frequency and duration of use/exposure	
• Maximum duration of exposure: > 240 min (not restricted) [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
Technical and organisational conditions and measures	
• Contact level: Intermittent	MEASE 1
• Pattern of exposure control: Direct handling	MEASE 1
• Pattern of use: Non-dispersive use	MEASE 1
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protective equipment (RPE) as precautionary measure: RPE protecting from local effects via inhalation	
• Gloves as precautionary measure: Gloves protecting from local effects to the skin (high hazard)	
• Eye protection: Eye protection to be worn to protect from adverse effects to the eyes	

9.2.5.2. Exposure and risks for workers

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table.

Table 9.22. Exposure concentrations and risks for workers

Route of exposure and type of effects	Assessment entity	Exposure concentration	Risk quantification
Inhalation, systemic, long term	tetraamminepalladium(2+) diacetate	10 µg/m³ (MEASE 1) RCR = 0.038	Final RCR = 0.038
Dermal, systemic, long term	tetraamminepalladium(2+) diacetate	34.29 µg/kg bw/day (MEASE 1) RCR = 0.095	Final RCR = 0.095
Combined routes, systemic, long-term			Final RCR = 0.134

Remarks on exposure data from external estimation tools:

MEASE 1 for tetraamminepalladium(2+) diacetate:
Explanation: Dermal, systemic, long term
For calculation of systemic exposure, the exposure estimate for total dermal loading as obtained in MEASE (reported in mg/day) is divided by a body weight of 70 kg for workers.

Risk characterisation

Qualitative risk characterisation (Inhalation, local, long term, Inhalation, local, acute, Dermal, local, long term, Dermal, local, acute, Eye, local):
Further information on the risk characterisation for local effects via inhalation, for local dermal effects and local effects to the eyes is given in Section 9.0.2.3.
Additional remarks on risk characterisation: Under the prescribed conditions of use, exposure is well below the DNELs and no local effects are expected. Therefore, risks are adequately controlled.

9.2.6. Worker CS 6: Fully contained reaction process (PROC 1)

Assessment entity group used for the assessment of this contributing scenario: tetraamminepalladium(2+) diacetate for OCC assessment

9.2.6.1. Conditions of use

	Method
Product (article) characteristics	
• Content in preparation: Not restricted [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
• Maximum emission potential of the substance: Very low	MEASE 1
• Physical form of substance: Solution	MEASE 1
Amount used (or contained in articles), frequency and duration of use/exposure	
• Maximum duration of exposure: > 240 min (not restricted) [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
Technical and organisational conditions and measures	
• Contact level: None	MEASE 1
• Level of containment: Closed process	MEASE 1
• Pattern of exposure control: Non-direct handling	MEASE 1
• Pattern of use: Closed system without breaches	MEASE 1
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protective equipment (RPE) as precautionary measure: RPE protecting from local effects via inhalation	
• Gloves as precautionary measure: Gloves protecting from local effects to the skin (high hazard)	
• Eye protection: Eye protection to be worn to protect from adverse effects to the eyes	

9.2.6.2. Exposure and risks for workers

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table.

Table 9.23. Exposure concentrations and risks for workers

Route of exposure and type of effects	Assessment entity	Exposure concentration	Risk quantification
Inhalation, systemic, long term	tetraamminepalladium(2+) diacetate	1 µg/m³ (MEASE 1) RCR = 3.85E-3	Final RCR < 0.01
Dermal, systemic, long term	tetraamminepalladium(2+) diacetate	1.71 µg/kg bw/day (MEASE 1) RCR = 4.75E-3	Final RCR < 0.01
Combined routes, systemic, long-term			Final RCR < 0.01

Remarks on exposure data from external estimation tools:

MEASE 1 for tetraamminepalladium(2+) diacetate:
Explanation: Dermal, systemic, long term
For calculation of systemic exposure, the exposure estimate for total dermal loading as obtained in MEASE (reported in mg/day) is divided by a body weight of 70 kg for workers.

Risk characterisation

Qualitative risk characterisation (Inhalation, local, long term, Inhalation, local, acute, Dermal, local, long term, Dermal, local, acute, Eye, local):
Further information on the risk characterisation for local effects via inhalation, for local dermal effects and local effects to the eyes is given in Section 9.0.2.3.
Additional remarks on risk characterisation: Under the prescribed conditions of use, exposure is well below the DNELs and no local effects are expected. Therefore, risks are adequately controlled.

9.2.7. Worker CS 7: Closed batch reaction process (PROC 3)

Assessment entity group used for the assessment of this contributing scenario: tetraamminepalladium(2+) diacetate for OCC assessment

9.2.7.1. Conditions of use

	Method
Product (article) characteristics	
• Content in preparation: Not restricted [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
• Maximum emission potential of the substance: Very low	MEASE 1
• Physical form of substance: Solution	MEASE 1
Amount used (or contained in articles), frequency and duration of use/exposure	
• Maximum duration of exposure: > 240 min (not restricted) [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
Technical and organisational conditions and measures	
• Contact level: Intermittent	MEASE 1
• Level of containment: Closed process	MEASE 1
• Pattern of exposure control: Non-direct handling	MEASE 1
• Pattern of use: Non-dispersive use	MEASE 1
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protective equipment (RPE) as precautionary measure: RPE protecting from local effects via inhalation	
• Gloves as precautionary measure: Gloves protecting from local effects to the skin (high hazard)	

	Method
• Eye protection: Eye protection to be worn to protect from adverse effects to the eyes	

9.2.7.2. Exposure and risks for workers

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table.

Table 9.24. Exposure concentrations and risks for workers

Route of exposure and type of effects	Assessment entity	Exposure concentration	Risk quantification
Inhalation, systemic, long term	tetraamminepalladium(2+) diacetate	10 µg/m³ (MEASE 1) RCR = 0.038	Final RCR = 0.038
Dermal, systemic, long term	tetraamminepalladium(2+) diacetate	1.71 µg/kg bw/day (MEASE 1) RCR = 4.75E-3	Final RCR < 0.01
Combined routes, systemic, long-term			Final RCR = 0.043

Remarks on exposure data from external estimation tools:

MEASE 1 for tetraamminepalladium(2+) diacetate:
Explanation: Dermal, systemic, long term
For calculation of systemic exposure, the exposure estimate for total dermal loading as obtained in MEASE (reported in mg/day) is divided by a body weight of 70 kg for workers.

Risk characterisation

Qualitative risk characterisation (Inhalation, local, long term, Inhalation, local, acute, Dermal, local, long term, Dermal, local, acute, Eye, local):
Further information on the risk characterisation for local effects via inhalation, for local dermal effects and local effects to the eyes is given in Section 9.0.2.3.
Additional remarks on risk characterisation: Under the prescribed conditions of use, exposure is well below the DNELs and no local effects are expected. Therefore, risks are adequately controlled.

9.2.8. Worker CS 8: Open or semi-closed wet chemical reaction process (PROC 4)

Assessment entity group used for the assessment of this contributing scenario: tetraamminepalladium(2+) diacetate for OCC assessment

9.2.8.1. Conditions of use

	Method
Product (article) characteristics	
• Content in preparation: Not restricted [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
• Maximum emission potential of the substance: Very low	MEASE 1
• Physical form of substance: Solution	MEASE 1
Amount used (or contained in articles), frequency and duration of use/exposure	
• Maximum duration of exposure: > 240 min (not restricted) [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
Technical and organisational conditions and measures	
• Contact level: Intermittent	MEASE 1
• Pattern of exposure control: Non-direct handling	MEASE 1
• Pattern of use: Non-dispersive use	MEASE 1
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protective equipment (RPE) as precautionary measure: RPE protecting	

	Method
from local effects via inhalation	
• Gloves as precautionary measure: Gloves protecting from local effects to the skin (high hazard)	
• Eye protection: Eye protection to be worn to protect from adverse effects to the eyes	

9.2.8.2. Exposure and risks for workers

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table.

Table 9.25. Exposure concentrations and risks for workers

Route of exposure and type of effects	Assessment entity	Exposure concentration	Risk quantification
Inhalation, systemic, long term	tetraamminepalladium(2+) diacetate	50 µg/m³ (MEASE 1) RCR = 0.192	Final RCR = 0.192
Dermal, systemic, long term	tetraamminepalladium(2+) diacetate	3.43 µg/kg bw/day (MEASE 1) RCR = 9.53E-3	Final RCR < 0.01
Combined routes, systemic, long-term			Final RCR = 0.202

Remarks on exposure data from external estimation tools:

MEASE 1 for tetraamminepalladium(2+) diacetate:
Explanation: Dermal, systemic, long term
For calculation of systemic exposure, the exposure estimate for total dermal loading as obtained in MEASE (reported in mg/day) is divided by a body weight of 70 kg for workers.

Risk characterisation

Qualitative risk characterisation (Inhalation, local, long term, Inhalation, local, acute, Dermal, local, long term, Dermal, local, acute, Eye, local):
Further information on the risk characterisation for local effects via inhalation, for local dermal effects and local effects to the eyes is given in Section 9.0.2.3.
Additional remarks on risk characterisation: Under the prescribed conditions of use, exposure is well below the DNELs and no local effects are expected. Therefore, risks are adequately controlled.

9.2.9. Worker CS 9: Laboratory analyses (PROC 15)

Assessment entity group used for the assessment of this contributing scenario: tetraamminepalladium(2+) diacetate for OCC assessment

9.2.9.1. Conditions of use

	Method
Product (article) characteristics	
• Content in preparation: Not restricted [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
• Maximum emission potential of the substance: Very low	MEASE 1
• Physical form of substance: Solution	MEASE 1
Amount used (or contained in articles), frequency and duration of use/exposure	
• Maximum duration of exposure: > 240 min (not restricted) [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
Technical and organisational conditions and measures	
• Contact level: Intermittent	MEASE 1
• Pattern of exposure control: Direct handling	MEASE 1
• Pattern of use: Non-dispersive use	MEASE 1

	Method
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protective equipment (RPE) as precautionary measure: RPE protecting from local effects via inhalation	
• Gloves as precautionary measure: Gloves protecting from local effects to the skin (high hazard)	
• Eye protection: Eye protection to be worn to protect from adverse effects to the eyes	

9.2.9.2. Exposure and risks for workers

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table.

Table 9.26. Exposure concentrations and risks for workers

Route of exposure and type of effects	Assessment entity	Exposure concentration	Risk quantification
Inhalation, systemic, long term	tetraamminepalladium(2+) diacetate	10 µg/m³ (MEASE 1) RCR = 0.038	Final RCR = 0.038
Dermal, systemic, long term	tetraamminepalladium(2+) diacetate	17.14 µg/kg bw/day (MEASE 1) RCR = 0.048	Final RCR = 0.048
Combined routes, systemic, long-term			Final RCR = 0.086

Remarks on exposure data from external estimation tools:

MEASE 1 for tetraamminepalladium(2+) diacetate:
Explanation: Dermal, systemic, long term
For calculation of systemic exposure, the exposure estimate for total dermal loading as obtained in MEASE (reported in mg/day) is divided by a body weight of 70 kg for workers.

Risk characterisation

Qualitative risk characterisation (Inhalation, local, long term, Inhalation, local, acute, Dermal, local, long term, Dermal, local, acute, Eye, local):
Further information on the risk characterisation for local effects via inhalation, for local dermal effects and local effects to the eyes is given in Section 9.0.2.3.
Additional remarks on risk characterisation: Under the prescribed conditions of use, exposure is well below the DNELs and no local effects are expected. Therefore, risks are adequately controlled.

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

Assessment entity group used for the assessment of this contributing scenario: tetraamminepalladium(2+) diacetate for OCC assessment

9.2.10.1. Conditions of use

	Method
Product (article) characteristics	
• Content in preparation: Not restricted [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
• Maximum emission potential of the substance: Very low	MEASE 1
• Physical form of substance: Solution	MEASE 1
Amount used (or contained in articles), frequency and duration of use/exposure	
• Maximum duration of exposure: > 240 min (not restricted) [Effectiveness Inhalation: 0%, Dermal: 0%]	MEASE 1
Technical and organisational conditions and measures	
• Contact level: Extensive	MEASE 1
• Immediate removal of splashes: Splashes should be removed immediately before	MEASE 1

	Method
drying of the substance	
• Pattern of exposure control: Direct handling	MEASE 1
• Pattern of use: Non-dispersive use	MEASE 1
Conditions and measures related to personal protection, hygiene and health evaluation	
• Respiratory protective equipment (RPE) as precautionary measure: RPE protecting from local effects via inhalation	
• Gloves: Protective gloves according to EN 374 have to be worn. Gloves have to be changed according to manufacturer's information or when damaged, whatever is the earlier. [Effectiveness Dermal: 90%]	MEASE 1
• Eye protection: Eye protection to be worn to protect from adverse effects to the eyes	

9.2.10.2. Exposure and risks for workers

The exposure concentrations and risk characterisation ratios (RCR) are reported in the following table.

Table 9.27. Exposure concentrations and risks for workers

Route of exposure and type of effects	Assessment entity	Exposure concentration	Risk quantification
Inhalation, systemic, long term	tetraamminepalladium(2+) diacetate	50 µg/m³ (MEASE 1) RCR = 0.192	Final RCR = 0.192
Dermal, systemic, long term	tetraamminepalladium(2+) diacetate	34.29 µg/kg bw/day (MEASE 1) RCR = 0.095	Final RCR = 0.095
Combined routes, systemic, long-term			Final RCR = 0.288

Remarks on exposure data from external estimation tools:

MEASE 1 for tetraamminepalladium(2+) diacetate:
Explanation: Dermal, systemic, long term
For calculation of systemic exposure, the exposure estimate for total dermal loading as obtained in MEASE (reported in mg/day) is divided by a body weight of 70 kg for workers.

Risk characterisation

Qualitative risk characterisation (Inhalation, local, long term, Inhalation, local, acute, Dermal, local, long term, Dermal, local, acute, Eye, local):
Further information on the risk characterisation for local effects via inhalation, for local dermal effects and local effects to the eyes is given in Section 9.0.2.3.
Additional remarks on risk characterisation: Under the prescribed conditions of use, exposure is well below the DNELs and no local effects are expected. Therefore, risks are adequately controlled.

10. RISK CHARACTERISATION RELATED TO COMBINED EXPOSURE

10.1. Human health

10.1.1. Workers

This chapter describes why a separate risk characterisation related to combined exposure is not required.
Combined exposure may result from any of the following scenarios:
1.Multiple palladium substances handled in parallel at the same workplace,
2.Inhalation and dermal exposure route contributing to systemic effects at the same time,
3.More than just a single contributing occupational exposure scenario relevant for an individual worker,
4.Workers that are also exposed to palladium substances in their free time
These scenarios are considered below:
1. Multiple palladium substances handled in parallel at the same workplace
Exposure monitoring data were obtained from a number of workplaces where palladium and/or palladium substances are manufactured or used in parallel. Any samples are analysed for their palladium content rather than for the content of the respective palladium substance. Thus, measured palladium levels are intrinsically reflective of any potential parallel exposure to multiple palladium substances and are not only relevant for a single palladium substance. An exposure assessment based on such monitoring data can therefore be considered to include an assessment for any palladium substance handled in parallel. For assessments based on modelling tools, it is noted that the handled amount is not considered as input parameter. For small-scale activities as relevant in the palladium industry, it can be assumed that these are covered for all substances handled in parallel by the exposure estimates, which refer to large scale and highly industrialised workplaces.
2. Inhalation and dermal exposure route contributing to systemic effects at the same time
A combined RCR is always maintained significantly below 1 in each of the ES.
3. More than just a single contributing occupational exposure scenario relevant for an individual worker
For aggregated exposure resulting from the applicability of more than just a single contributing worker scenario in a single work shift, it is noted that allexposure levels were derived for a full-shift exposure time and a safe use was demonstrated for each contributing scenario. Thus, by demonstrating safe use for individual contributing scenarios it is assured that a combination of activities within a single shift, could not exceed the highest calculated RCRfor any of the individual activities in that shift.
4. Workers that are also exposed to palladium substances in their free time (e.g. as member of the general population or as consumer)
For workers who are members of other populations to be protected in this chemical safety assessment (i.e. general population), a specific combined exposure assessment is not required as workers represent a less vulnerable population in comparison to subpopulations (e.g. children) which may be considered in assessments for the general population. Any RCR from these subpopulations could safely be assumed to be in fact significantly lower if re-calculated for workers. In a combined assessment of exposures one would also avoid adding the worst case RCR for workers with the worst case RCR of another population as this would lead to an unrealistic scenario. Instead typical RCRs would be taken which would in combination lead to a low combined RCR.

10.1.2. Consumer

10.2. Environment (combined for all emission sources)

10.2.1. All uses (regional scale)

10.2.1.1. Total releases

The total releases to the environment from all the exposure scenarios covered are presented in the table below. This is the sum of the releases to the environments from all exposure scenarios addressed.
Where there is more than one contributing scenario for the environment for a given exposure scenario, the highest release per route across all the contributing scenarios within the use has been taken into account as the release for the use (both for the regional and the exposure due to all the widespread uses). This may lead to overestimation of the PEC.

Table 10.1. Total releases to the environment per year from all life cycle stages

Release route	Assessment entity	Total releases per year
Water	Pd dissolved	3.147 kg/year
Air	Pd dissolved	1.68 kg/year
Soil	Pd dissolved	0 kg/year

10.2.2. Regional assessment

The regional predicted environmental concentration (PEC regional) and the related risk characterisation ratios when a PNEC is available are presented in the table below. The exposure to man via the environment from regional exposure and the related risk characterisation ratios are also provided (when relevant). The exposure concentration for human via inhalation is equal to the PEC air.
The exposure estimates have been obtained with EUSES 2.1.2 unless stated otherwise.

Table 10.2. Predicted regional exposure concentrations (Regional PEC) and risks for the environment

Protection target	Assessment entity	Regional PEC	Risk characterisation
Fresh water	Pd dissolved	**Regional PEC:** 1.75E-7 mg/L (estimated by External EUSES calculation 2.1.2) RCR = 3.89E-3	Final RCR < 0.01
Sediment (freshwater)	Pd dissolved	**Regional PEC:** 1.53E-3 mg/kg dw (estimated by External EUSES calculation 2.1.2) RCR = 5.58E-3	Final RCR < 0.01
Marine water	Pd dissolved	**Regional PEC:** 1.7E-8 mg/L (estimated by External EUSES calculation 2.1.2) RCR = 3.78E-3	Final RCR < 0.01
Sediment (marine water)	Pd dissolved	**Regional PEC:** 1.52E-4 mg/kg dw (estimated by External EUSES calculation 2.1.2) RCR = 5.55E-3	Final RCR < 0.01
Agricultural soil	Pd dissolved	**Regional PEC:** 1.85E-3 mg/kg dw (Measured data: GEMAS) RCR = 0.094	Final RCR = 0.094

Remarks on risk characterisation for regional concentrations:

To derive the regional background concentration for environmental compartments two approaches have been followed; EUSES modelling based on regional production volume for the aquatic environment, and data from peer-reviewed, published literature for the terrestrial compartment.
For the derivation of the regional background concentrations in the aquatic environment, the total tonnage of all palladium (Pd) compounds produced in the EU was sub-divided by region. The value input to modelling was the maximum proportion of Pd compounds produced in a single region. This regional assumption was combined with emission characteristics from the Pd manufacturing and processing sector data, STP removal efficiency and phys-chem properties to perform calculations of the regional PEC concentrations for freshwater and freshwater sediment and marine water and sediment. The estimated regional background PECs were then incorporated into all GESs.
For the derivation of regional background concentrations in the terrestrial environment, data from the geochemical mapping of agricultural and grazing land soil of Europe (GEMAS) project were utilised. GEMAS is a project conducted by the EuroGeoSurveys Geochemistry Expert Group and Eurometaux for the production of exposure data on metals in agricultural and grazing land soil and soil properties, at the European scale.

10.2.3. Local exposure due to all widespread uses

Not relevant as there are not several widespread uses covered in this CSR.

Annexes

1. Annex: References

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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:**

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:**

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:**

Details on test material: 10000 ppm Pd(II) plasma emission standard in 1.2 M HCl Source: BDH

Test material: **134620-00-1 / 134620-00-1; Tetraammine palladium hydrogen carbonate**
Form: **not specified**

Composition type: Constituent	**Reference substance:** Tetraammine palladium hydrogen carbonate EC no.: CAS no: IUPAC name: Tetraammine palladium hydrogen carbonate	**Concentration range:**
Composition type: Constituent	**Reference substance:** 134620-00-1 EC no.: CAS no: 134620-00-1 IUPAC name: 134620-00-1	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): Tetrammine palladium hydrogen carbonate - Substance type: no data - Physical state: no data - Analytical purity: no data - Lot/batch No.: no data - Stability under test conditions: no data - Storage condition of test material: no data

Test material: **61495-96-3 / 262-819-1; Tetraamminepalladium diacetate**
Form: **liquid**

Composition type: Constituent	**Reference substance:** Tetraamminepalladium diacetate EC no.: CAS no: IUPAC name: Tetraamminepalladium diacetate	**Concentration range:**
Composition type: Constituent	**Reference substance:** Tetraamminepalladium(2+) diacetate EC no.: 262-819-1 CAS no: 61495-96-3 IUPAC name: Tetraamminepalladium(2+) diacetate	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): Tetraamminepalladium (II) acetate -

Substance type: No data - Physical state: Yellow liquid - Analytical purity: No data - Impurities (identity and concentrations): Chlorine (0.022%). Less than 100 ppm calcium, and less than 50 ppm gold, copper, iron, iridium, magnesioum, lead, platinum, rhodium ruthenium and silicon are reported in the certificate of analysis. - Composition of test material, percentage of components: Tetraamminepalladium(II) acetate solution (44.16% w/w/; 16.06% w/w palladium content) - Isomers composition: No data - Purity test date: No data - Lot/batch No.: 7300/34-10 - Expiration date of the lot/batch: Retest date: July 2015 - Stability under test conditions: No data - Storage condition of test material: 15-25 deg C in a sealed container, protected from direct sunlight

Test material: **134620-00-1 / 134620-00-1; Tetramminepalladium (II) hydrogen carbonate**
Form: **solid**

Composition type: Constituent	**Reference substance:** Tetramminepalladium (II) hydrogen carbonate EC no.: CAS no: IUPAC name: Tetramminepalladium (II) hydrogen carbonate	**Concentration range:**
Composition type: Constituent	**Reference substance:** 134620-00-1 EC no.: CAS no: 134620-00-1 IUPAC name: 134620-00-1	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): Tetrammine palladium hydrogen carbonate - Substance type: No data - Physical state: pale yellow solid - 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.: DF0445 - Expiration date of the lot/batch: No data - Stability under test conditions: No data - Storage condition of test material: ambient temperature, shielded from light

Test material: **13815-17-3 / 237-489-7; Tetraamminepalladium dichloride**
Form:

Composition type: Constituent	**Reference substance:** Tetraamminepalladium dichloride EC no.: CAS no: IUPAC name: Tetraamminepalladium dichloride	**Concentration range:**
Composition type: Constituent	**Reference substance:** Tetraamminepalladium(2+) dichloride EC no.: 237-489-7 CAS no: 13815-17-3 IUPAC name: Tetraamminepalladium(2+) dichloride	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): tetraamminepalladous chloride - Substance type: light yellow crystalline powder - Physical state: solid - Analytical purity: no data - Impurities (identity and concentrations): no data - Purity test date: no data - Lot/batch No.: 041232 - Expiration date of the lot/batch: no data - Stability under test conditions: no data - Storage condition of test material: no data

Test material: **134620-00-1 / 134620-00-1; Tetraamminepalladium hydrogen carbonate**
Form: **not specified**

Composition type: Constituent	**Reference substance:** Tetraamminepalladium hydrogen carbonate EC no.: CAS no: IUPAC name: Tetraamminepalladium hydrogen	**Concentration range:**

	carbonate	
Composition type: Constituent	**Reference substance:** 134620-00-1 EC no.: CAS no: 134620-00-1 IUPAC name: 134620-00-1	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): Tetrammine palladium hydrogen carbonate - Substance type: no data - Physical state: no data - Analytical purity: no data - Lot/batch No.: no data - Stability under test conditions: no data - Storage condition of test material: no data

Test material: **61495-96-3 / 262-819-1; Tetramminepalladium diacetate**
Form: **aqueous solution**

Composition type: Constituent	**Reference substance:** Tetramminepalladium diacetate EC no.: CAS no: IUPAC name: Tetramminepalladium diacetate	**Concentration range:**
Composition type: Constituent	**Reference substance:** Tetraamminepalladium(2+) diacetate EC no.: 262-819-1 CAS no: 61495-96-3 IUPAC name: Tetraamminepalladium(2+) diacetate	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): tetraamminepalladium(II) acetate solution. - Substance type: aqueous solution. - Physical state: liquid. - Analytical purity: 44.16% w/w tetraamminepalladium(II) acetate. - Impurities (identity and concentrations): no data. - Composition of test material, percentage of components: 16.06% palladium. - Isomers composition: not applicable. - Purity test date: 21 July 2014. - Lot/batch No.: 7300/34-10. - Expiration date of the lot/batch: 21 July 2015. - Stability under test conditions: no data. - Storage condition of test material: controlled room temperature (15-25 deg C, below 70 RH%). Store in tightly-closed original container, protected from light, in a dry, cool and well-ventilated area.

Test material: **13815-17-3 / 237-489-7; Tetraamminepalladium (II) dichloride**
Form: **solid: particulate/powder - migrated information: powder**

Composition type: Constituent	**Reference substance:** Tetraamminepalladium (II) dichloride EC no.: CAS no: IUPAC name: Tetraamminepalladium (II) dichloride	**Concentration range:**
Composition type: Constituent	**Reference substance:** Tetraamminepalladium(2+) dichloride EC no.: 237-489-7 CAS no: 13815-17-3 IUPAC name: Tetraamminepalladium(2+) dichloride	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): tetraamminepalladous chloride - Substance type: yellow powder - Physical state: solid - Analytical purity: no data - Impurities (identity and concentrations): no data - Composition of test material, percentage of components: no data - Purity test date: no data - Lot/batch No.: 041232 - Expiration date of the lot/batch: no data - Stability under test conditions: no data - Storage condition of test material: no data

Test material: **134620-00-1 / 134620-00-1; Tetramminepalladium hydrogen carbonate**
Form: **solid: particulate/powder - migrated information: powder**

Composition type: Constituent	**Reference substance:** Tetramminepalladium hydrogen	**Concentration range:**

	carbonate EC no.: CAS no: IUPAC name: Tetramminepalladium hydrogen carbonate	
Composition type: Constituent	**Reference substance:** 134620-00-1 EC no.: CAS no: 134620-00-1 IUPAC name: 134620-00-1	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): Tetrammine palladium hydrogen carbonate - Substance type: No data - Physical state: pale yellow powder - 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.: DD0274 - Expiration date of the lot/batch: No data - Stability under test conditions: No data - Storage condition of test material: room temperature

Test material: **13815-17-3 / 237-489-7; Tetraamminepalladium dichloride**
Form:

Composition type: Constituent	**Reference substance:** Tetraamminepalladium dichloride EC no.: CAS no: IUPAC name: Tetraamminepalladium dichloride	**Concentration range:**
Composition type: Constituent	**Reference substance:** Tetraamminepalladium(2+) dichloride EC no.: 237-489-7 CAS no: 13815-17-3 IUPAC name: Tetraamminepalladium(2+) dichloride	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): tetraammine palladium chloride - Substance type: pale yellow crystalline solid - Physical state: solid - 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.: DK0164 - Expiration date of the lot/batch: no data - Stability under test conditions: no data - Storage condition of test material: room temperature in dark

Test material: **134620-00-1 / 134620-00-1; Tetraamminepalladium hydrogen carbonate**
Form:

Composition type: Constituent	**Reference substance:** Tetraamminepalladium hydrogen carbonate EC no.: CAS no: IUPAC name: Tetraamminepalladium hydrogen carbonate	**Concentration range:**
Composition type: Constituent	**Reference substance:** 134620-00-1 EC no.: CAS no: 134620-00-1 IUPAC name: 134620-00-1	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): Tetrammine palladium hydrogen carbonate - Substance type: no data - Physical state: no data - Analytical purity: no data - Lot/batch No.: no data - Stability under test conditions: no data - Storage condition of test material: no data

Test material: **13815-17-3 / 237-489-7; Tetraamminepalladium dichloride**

Form: **solid**

Composition type: Constituent	**Reference substance:** Tetraamminepalladium dichloride EC no.: CAS no: IUPAC name: Tetraamminepalladium dichloride	**Concentration range:**
Composition type: Constituent	**Reference substance:** Tetraamminepalladium(2+) dichloride EC no.: 237-489-7 CAS no: 13815-17-3 IUPAC name: Tetraamminepalladium(2+) dichloride	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): Tetraamminepalladium(2+) dichloride - Physical state: solid - Analytical purity: Pd content: 41.69% - Impurities (identity and concentrations): 15 ppm Pt; <2 ppm Ru, <5 ppm Rh; <10 ppm Ir; 4 ppm Au; 7 ppm Ag; 3 ppm Al; 1 ppm Ca; <2 ppm Co; <1 ppm Cr; 13 ppm Cu; <2 ppm Fe; <2 pmm Mg; <5 ppm Mn; <1 ppm Ni; <2 ppm Pb; <10 ppm Sb; <10 ppm Si; <5 ppm Sn; 18 ppm Zn. - Isomers composition: not applicable - Purity test date: - Lot/batch No.: 10214 - Expiration date of the lot/batch: 13 January 2015 - Stability under test conditions: The test item solution in aqueous ammonium-chloride buffer was stable over 7 days at room temperature and for 14 days when refrigerated (2-8ºC). - Storage condition of test material: Controlled room temperature (15-25 deg C, below 70 RH%), protected from humidity

Test material: **134620-00-1 / 134620-00-1; Tetrammine Palladium Hydrogen Carbonate**
Form: **solid: particulate/powder - migrated information: powder**

Composition type: Constituent	**Reference substance:** Tetrammine Palladium Hydrogen Carbonate EC no.: CAS no: IUPAC name: Tetrammine Palladium Hydrogen Carbonate	**Concentration range:**
Composition type: Constituent	**Reference substance:** 134620-00-1 EC no.: CAS no: 134620-00-1 IUPAC name: 134620-00-1	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): tetrammine palladium hydrogen carbonate - Substance type: no data - Physical state: pale yellow solid - 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.: DF0445 - Expiration date of the lot/batch: no data - Stability under test conditions: formulations prepared weekly were stable for at least 10 days - Storage condition of test material: compound stored at room temperature, shielded from light; formulations stored at approximately 4 °C, in the dark

Test material: **134620-00-1 / 134620-00-1; Tetramminepalladium hydrogen carbonate**
Form: **solid: particulate/powder - migrated information: powder**

Composition type: Constituent	**Reference substance:** Tetramminepalladium hydrogen carbonate EC no.: CAS no: IUPAC name: Tetramminepalladium hydrogen carbonate	**Concentration range:**
Composition type: Constituent	**Reference substance:** 134620-00-1 EC no.: CAS no: 134620-00-1 IUPAC name: 134620-00-1	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): Tetrammine palladium hydrogen

carbonate - Substance type: No data - Physical state: pale yellow powder - 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.: DD0247 - Expiration date of the lot/batch: No data - Stability under test conditions: No data - Storage condition of test material: room temperature

Test material: **134620-00-1 / 134620-00-1; Tetraamminepalladium hydrogen carbonate**
Form: **not specified**

Composition type: Constituent	**Reference substance:** Tetraamminepalladium hydrogen carbonate EC no.: CAS no: IUPAC name: Tetraamminepalladium hydrogen carbonate	**Concentration range:**
Composition type: Constituent	**Reference substance:** 134620-00-1 EC no.: CAS no: 134620-00-1 IUPAC name: 134620-00-1	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): Tetrammine palladium hydrogen carbonate

Test material: **13815-17-3 / 237-489-7; Tetraamminepalladium dichloride**
Form:

Composition type: Constituent	**Reference substance:** Tetraamminepalladium dichloride EC no.: CAS no: IUPAC name: Tetraamminepalladium dichloride	**Concentration range:**
Composition type: Constituent	**Reference substance:** Tetraamminepalladium(2+) dichloride EC no.: 237-489-7 CAS no: 13815-17-3 IUPAC name: Tetraamminepalladium(2+) dichloride	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): Tetraamminepalladium(2+) dichloride - Physical state: solid - Analytical purity: Pd content: 41.69% - Impurities (identity and concentrations): 15 ppm Pt; <2 ppm Ru, <5 ppm Rh; <10 ppm Ir; 4 ppm Au; 7 ppm Ag; 3 ppm Al; 1 ppm Ca; <2 ppm Co; <1 ppm Cr; 13 ppm Cu; <2 ppm Fe; <2 pmm Mg; <5 ppm Mn; <1 ppm Ni; <2 ppm Pb; <10 ppm Sb; <10 ppm Si; <5 ppm Sn; 18 ppm Zn. - Isomers composition: not applicable - Purity test date: - Lot/batch No.: 10214 - Expiration date of the lot/batch: 13 January 2015 - Stability under test conditions: The test item solution in aqueous ammonium-chloride buffer was stable over 7 days at room temperature and for 14 days when refrigerated (2-8ºC). - Storage condition of test material: Controlled room temperature (15-25 deg C, below 70 RH%), protected from humidity

Test material: **13815-17-3 / 237-489-7; Tetraamminepalladium dichloride**
Form:

Composition type: Constituent	**Reference substance:** Tetraamminepalladium dichloride EC no.: CAS no: IUPAC name: Tetraamminepalladium dichloride	**Concentration range:**
Composition type: Constituent	**Reference substance:** Tetraamminepalladium(2+)	**Concentration range:**

	dichloride EC no.: 237-489-7 CAS no: 13815-17-3 IUPAC name: Tetraamminepalladium(2+) dichloride	

Details on test material: - Name of test material (as cited in study report): Tetraamminepalladium(2+) dichloride - Substance type: - Physical state: solid - Analytical purity: Pd content: 41.69% - Impurities (identity and concentrations): 15 ppm Pt; <2 ppm Ru, <5 ppm Rh; <10 ppm Ir; 4 ppm Au; 7 ppm Ag; 3 ppm Al; 1 ppm Ca; <2 ppm Co; <1 ppm Cr; 13 ppm Cu; <2 ppm Fe; <2 pmm Mg; <5 ppm Mn; <1 ppm Ni; <2 ppm Pb; <10 ppm Sb; <10 ppm Si; <5 ppm Sn; 18 ppm Zn. - Isomers composition: not applicable - Purity test date: 16 January 2014 - Lot/batch No.: 10214 - Expiration date of the lot/batch: 13 January 2015 - Stability under test conditions: The test item solution in aqueous ammonium-chloride buffer was stable over 7 days at room temperature and for 14 days when refrigerated (2-8ºC). - Storage condition of test material: Controlled room temperature (15-25 deg C, below 70 RH%), protected from humidity

Test material: **Tetraamminepalladium (II) acetate**
Form: **solid: particulate/powder**

Composition type:	**Reference substance:**	**Concentration range:**
Constituent	Tetraamminepalladium(2+) diacetate EC no.: 262-819-1 CAS no: 61495-96-3 IUPAC name: Tetraamminepalladium(2+) diacetate	

Details on test material: Name: Tetraamminepalladium (II) acetate Cas No: 61495-96-3 Physical state: soild powder

Test material: **14323-43-4 / 238-269-3**
Form: **solid: particulate/powder - migrated information: powder**

Composition type:	**Reference substance:**	**Concentration range:**
Constituent	Diamminedichloropalladium EC no.: 238-269-3 CAS no: 14323-43-4 IUPAC name: Diamminedichloropalladium	

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: **134620-00-1 / 134620-00-1; Tetrammine Palladium Hydrogen Carbonate**
Form:

Composition type:	**Reference substance:** 134620-00-1	**Concentration range:**
Constituent	EC no.: CAS no: 134620-00-1 IUPAC name: 134620-00-1	
Composition type:	**Reference substance:** Tetrammine	**Concentration range:**
Constituent	Palladium Hydrogen Carbonate EC no.: CAS no: IUPAC name: Tetrammine Palladium Hydrogen Carbonate	

Details on test material: Pale yellow solid, batch No DF0445 received on 12 August 1996 and stored at room temperature shielded from light (not necessarily in darkness).

Test material: **Dihydrogen tetrachloropalladate**
Form:

Composition type: Constituent	**Reference substance:** Dihydrogen tetrachloropalladate EC no.: 241-047-9 CAS no: 16970-55-1 IUPAC name: Dihydrogen tetrachloropalladate	**Concentration range:**

Test material: **Diamminedichloropalladium (II)**
Form: **solid: particulate/powder - migrated information: powder**

Composition type: Constituent	**Reference substance:** Diamminedichloropalladium (II) EC no.: CAS no: IUPAC name: Diamminedichloropalladium (II)	**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: **Dihydrogen tetrachloropalladate (II); palladium(4+) tetrachloride / 16970-55-1 / 241-047-9**
Form: **liquid**

Composition type: Constituent	**Reference substance:** Dihydrogen tetrachloropalladate EC no.: 241-047-9 CAS no: 16970-55-1 IUPAC name: Dihydrogen tetrachloropalladate	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): Dihydrogen tetrachloropalladate (II) (in hydrochloric acid) - Substance type: No data - Physical state: Brown liquid - Analytical purity: No data - Impurities (identity and concentrations): Pt (30 ppm); Rh (14 ppm); Ag (9 ppm); Cu (2 ppm); Fe (2 ppm); Pb (3 ppm); Sb (20 ppm); Ru, Ir, Au, Al, Ca, Co, Cr, Mg, Mn, Ni, Si, Sn and Zn (< detection limit) - Composition of test material, percentage of components: Dihydrogen tetrachloropalladate (II) in hydrochloric acid (52.41% w/v; 22.29% w/w palladium content) - Isomers composition: No data - Purity test date: 24 July 2014 - Lot/batch No.: 12614 - Expiration date of the lot/batch: 15 April 2015 - Storage condition of test material: 15-25 deg C, protected from light

Test material: **14323-43-4 / 238-269-3; Diamminedichloropalladium (II)**
Form: **solid: particulate/powder - migrated information: powder**

Composition type: Constituent	**Reference substance:** Diamminedichloropalladium (II) EC no.: CAS no: IUPAC name: Diamminedichloropalladium (II)	**Concentration range:**
Composition type: Constituent	**Reference substance:** Diamminedichloropalladium EC no.: 238-269-3 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: 50.35% Palladium - Lot/batch No.: 10912 - Expiration date of the lot/batch: 28 August 2014 - 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:**

Test material: **14323-43-4 / 238-269-3**
Form: **solid: particulate/powder - migrated information: powder**

Composition type: Constituent	**Reference substance:** Diamminedichloropalladium EC no.: 238-269-3 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: **Palladium dichloride dihydrate; palladium(2+) dichloride / 7647-10-1 / 231-596-2**
Form: **not specified**

Composition type: Constituent	**Reference substance:** Palladium dichloride dihydrate EC no.: CAS no: IUPAC name: Palladium dichloride dihydrate	**Concentration range:**
Composition type: Constituent	**Reference substance:** Palladium dichloride EC no.: 231-596-2 CAS no: 7647-10-1 IUPAC name:	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): PdCl2.2(H2O) - 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: **134620-00-1 / 134620-00-1; Tetrammine Palladium Hydrogen Carbonate**
Form:

Composition type: Constituent	**Reference substance:** 134620-00-1 EC no.: CAS no: 134620-00-1 IUPAC name: 134620-00-1	**Concentration range:**
Composition type: Constituent	**Reference substance:** Tetrammine Palladium Hydrogen Carbonate EC no.: CAS no: IUPAC name: Tetrammine Palladium Hydrogen Carbonate	**Concentration range:**

Details on test material: Pale yellow solid, batch No DF0445 received on 12 August 1996 and stored at room temperature shielded from light (not necessarily in darkness).

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

Form: **solid**

Composition type: Constituent	**Reference substance:** palladium dichloride EC no.: 231-596-2 CAS no: 7647-10-1 IUPAC name: palladium(2+) dichloride	**Concentration range:**

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

Composition type: Constituent	**Reference substance:** palladium dichloride EC no.: 231-596-2 CAS no: 7647-10-1 IUPAC name: palladium(2+) dichloride	**Concentration range:**

Test material: **14323-43-4 / 238-269-3**
Form: **solid: particulate/powder - migrated information: powder**

Composition type: Constituent	**Reference substance:** Diamminedichloropalladium EC no.: 238-269-3 CAS no: 14323-43-4 IUPAC name: Diamminedichloropalladium	**Concentration range:**

Details on test material: - Name of test material (as cited in study report): Diamminedichloropalladium - Molecular formula (if other than submission substance): C12H6N2Pd - Molecular weight (if other than submission substance): 211.39 g/mol - 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: Closed dry vessel at room temperature

Test material: **134620-00-1 / 134620-00-1; Tetrammine Palladium Hydrogen Carbonate**
Form:

Composition type: Constituent	**Reference substance:** 134620-00-1 EC no.: CAS no: 134620-00-1 IUPAC name: 134620-00-1	**Concentration range:**
Composition type: Constituent	**Reference substance:** Tetrammine Palladium Hydrogen Carbonate EC no.: CAS no: IUPAC name: Tetrammine Palladium Hydrogen Carbonate	**Concentration range:**

Details on test material: Pale yellow solid, batch No DD0247 received on 25 January 1995 and stored at room temperature in a black plastic tube.

3. Annex: Mode of action / Human relevance Framework

Section 5.6.3: Repeated dose toxicity
Detailed information on mode of action / Human relevance framework:

Section 5.7.3: Genetic toxicity
Detailed information on mode of action / Human relevance framework:

Section 5.9.3: Toxicity to reproduction
Detailed information on mode of action / Human relevance framework: