INTERNATIONAL PLATINUM GROUP METALS ASSOCIATION

Platinum Group Metals and their compounds:

Summary Toxicity and Hazard Classification information collated principally from EU REACH Registration dossiers

Disclaimer

This document has been prepared by toxicologists working in the platinum group metals (PGM) industry, principally based on toxicity data and hazard classification information contained within the corresponding REACH registration dossiers published by the European Chemicals Agency (ECHA) and prepared by the European Precious Metals Federation (info@epmf.be). The authors have aimed to faithfully represent the information published by ECHA, at the time of writing, in a concise and helpful format. This reflects the best knowledge on these substances developed by the EPMF and IPA. No warranty is provided for the accuracy of the data published by ECHA nor as reflected in this document. New toxicity data continue to be generated on PGM substances and hazard classifications for individual substances or groups of substances may change. This document is not and should not be construed to be either comprehensive nor advice or recommendation of any kind. Neither the contributors to this document nor the International Platinum Group Metals Association assumes any liability for any errors or omissions or for any personal injury, physical harm, or any loss or damages of whatsoever nature arising from or in connection with the use of the information contained within this document.

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1. Introduction

The International Platinum Group Metals Association (IPA) publication 'Safe Use of Platinum Group Metals in the Workplace' provides an extensive review of information relevant to protecting the health of workers occupationally exposed to platinum group metal (PGM) substances, with particular focus on the predominant health concern that is platinum salt sensitivity (PSS). The document comprises the following 10 chapters:

1. Introduction and Executive Summary
2. Physical and Chemical Properties of PGMs
3. Production and Uses of PGMs
4. Sources of Exposure to PGMs
5. Toxicokinetics of Platinum and other PGMs
6. Toxicity of Platinum and Platinum Compounds with Summaries for other PGMs
7. Medical Surveillance of Workers Exposed to Respiratory Sensitising Platinum Compounds
8. Workplace Monitoring
9. Control Measures and Management Systems
10. Workplace Regulatory Systems and Hazard Communication

Since the publication of that document in 2017, a range of new toxicity data have been generated for various PGM substances, largely as a consequence of the requirements of the EU REACH Regulation on the Registration, Evaluation, Authorisation and Restriction of Chemicals.

The present document has been prepared to complement and supplement Chapter 6 of the workplace guidance document by providing concise summaries of the human health toxicity data and hazard classifications of the PGM substances that have been Registered under EU REACH.

The toxicity data summaries and hazard classification tables presented in this document were compiled from a combination of data contained within the Lead registration dossier for each substance as published by the European Chemicals Agency (ECHA) on its ECHA-CHEM portal, as well as supplementary information held by the European Precious Metals Federation (EPMF) that, at the time of authoring, is not yet available via the ECHA-CHEM portal (i.e., yet to be submitted to ECHA, or yet to be published by ECHA).

Data and hazard classifications are provided for various platinum, palladium, rhodium, ruthenium, and iridium substances. No osmium substances have been registered under the EU REACH Regulation and no toxicity data for any osmium substances are available on the ECHA-CHEM website. Similarly, other forms of PGM that are not covered by the published REACH Registration dossiers, including platinum-based antineoplastic chemotherapy drugs and nanoforms of PGM metals or compounds, are beyond the remit of this document.

As a supplement to the workplace guidance document, this document is a compilation of human health toxicity and hazard classification endpoints only; physical-chemical hazards and ecotoxicological data and hazard classifications are not described.

For each metal, substances have generally been grouped according to similar physical-chemical and toxicological properties. This does not mean that all substances that would fit within a group based on physicochemical properties will necessarily share the same toxicological properties. Hence, extrapolation of toxicological properties to substances not covered in this document should be avoided. Importantly, while the grouping of substances under EU REACH may be generally aligned

with the framework provided herein, there may be important differences and further sub-categorisation of substances within the EU REACH framework based on additional considerations such as ion release dynamics or specific hazard characteristics.

Before working with any PGM substance, a suitable risk assessment should be completed by an appropriately qualified person using up-to-date information, including that contained in the Safety Data Sheet (SDS).

2. Platinum metal and its compounds

2.1. Introduction and summary

Active EU REACH Registration dossiers for 17 platinum substances were identified.[1] A further platinum substance, diammonium hexachloroplatinate, which has an inactive dossier due to cessation of manufacture in the EU, has been included as it is similar to other platinum substances with active registrations and it has toxicity testing data helpful in providing understanding of the hazard profile of these types of platinum substances. An overview of the human health hazard classifications and toxicity dataset for these 18 substances is provided in Table 1. For this purpose, the substances have been grouped as follows:

- Elemental platinum and platinum oxides
- Hexahydroxyplatinum substances
- Tetraammineplatinum substances
- Complex halogenated platinum substances (chloroplatinates)
- Other platinum substances – monoconstituent substances
- Other platinum substances – UVCBs (unknown or variable composition, complex reaction products or of biological materials)

The main health hazard associated with certain platinum substances is respiratory sensitisation. This is discussed in much greater detail in the 2017 IPA publication 'Safe Use of Platinum Group Metals in the Workplace'.

Across the 18 platinum substances covered herein, only the four chloroplatinate substances are classified for respiratory sensitisation potential (Cat 1A). The propensity of chloroplatinates to cause sensitisation of the respiratory tract has been known for a long time. This has been conclusively demonstrated by various occupational epidemiology studies while equivalent studies have been helpful in demonstrating other types of Pt substances, such as the tetraammineplatinum substances, do not possess this ability.

2.2. Elemental platinum and platinum oxides

This group comprises elemental platinum, platinum oxide, and platinum dioxide (and hydrate). These forms of platinum are considered to be largely inert and non-bioavailable.

Substance	CAS number	Chemical structure
Platinum	7440-06-4	Pt
Platinum oxide	12035-82-4	Pt=O
Platinum dioxide (and hydrate)	1314-15-4	O=Pt=O

[1] An active dossier for an additional platinum substance (1,5-Cyclooctadienyl-bis[4-(trimethylsilyl)phenyl]ethinyl platinum, EC# 460-090-6) was also identified, but it contained virtually no useful information.

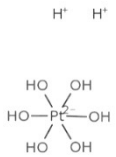
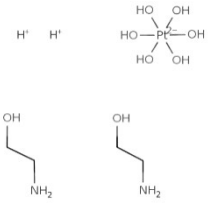
Elemental platinum has data for acute toxicity, in-vitro skin and eye irritation, three in vitro genotoxicity tests (as well as an additional genotoxicity study judged to be unreliable), and a reproductive toxicity screening study (similar to OECD test guideline 422). No hazard classifications have been assigned. Lack of hazard classifications is further supported by transformation/dissolution tests (a general indicator of ion release in aquatic media) indicating elemental platinum will have negligible bioavailability. For some endpoints, read-across of data for platinum dioxide is utilized. In addition, these conclusions are supported by bioelution data available on Pt and Pt-black.

Platinum oxide has no toxicity data and no hazard classifications assigned.

Platinum dioxide has a dataset comprising acute oral toxicity, skin irritation, eye irritation, skin sensitisation, plus limited genotoxicity testing. Additional genotoxicity testing on platinum metal powder was used in a read-across approach to provide supplemental data. The results of the studies did not require any hazard classifications to be assigned.

2.3. Hexahydroxyplatinum substances

The hexahydroxyplatinum substances group comprises dihydrogen hexahydroxyplatinate, and dihydrogen hexahydroxyplatinate compound with 2-aminoethanol (1:2).

Substance	CAS number	Chemical structure
dihydrogen hexahydroxyplatinate	51850-20-5	
dihydrogen hexahydroxyplatinate compound with 2-aminoethanol (1:2)	68133-90-4	

The toxicity dataset for this group comprises studies of acute oral toxicity, skin irritation, eye irritation, skin sensitisation, mutagenicity, and general repeated dose, reproductive and developmental toxicity.

Dihydrogen hexahydroxyplatinate was not irritating to skin and was a Cat 2 eye irritant; whereas, dihydrogen hexahydroxyplatinate compound with 2-aminoethanol (1:2) was corrosive to skin (Cat 1b) and based partially on in vitro eye irritation data and the skin corrosion classification a classification of Eye Damage Cat 1 was assigned.

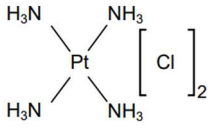
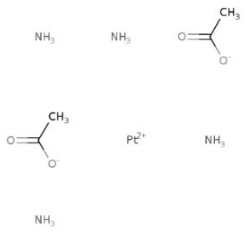
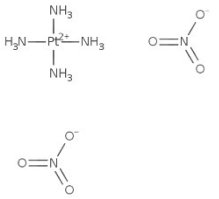
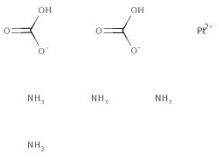
For each substance, the results of studies of acute oral toxicity, skin sensitisation, mutagenicity, and general repeated dose, reproductive and developmental toxicity (screening study) did not require classification for those endpoints.

Each of the in vitro genotoxicity studies available for dihydrogen hexahydroxyplatinate (in vitro bacterial reverse mutation assay and in vitro mammalian cell micronucleus assay) and dihydrogen hexahydroxyplatinate compound with 2-aminoethanol (1:2) (in vitro bacterial reverse mutation assay

and in vitro mammalian cell gene mutation test) showed evidence of genotoxicity, but an in vivo combined comet and micronucleus test of dihydrogen hexahydroxyplatinate compound with 2-aminoethanol (1:2) was negative and this result was also read-across to dihydrogen hexahydroxyplatinate to conclude no classification for mutagenicity is required for either substance.

2.4. Tetraammineplatinum substances

This group comprises the dichloride, diacetate, dinitrate, and hydrogen carbonate salts of tetraammineplatinum.

Substance	CAS number	Chemical structure
Tetraammine platinum dichloride	13933-32-9	
Tetraammine platinum (II) diacetate	127733-97	
Tetraammine platinum dinitrate	20634-12-2	
Tetraammine platinum (II) hydrogen carbonate	123439-82-7	

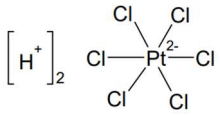
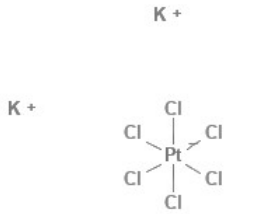
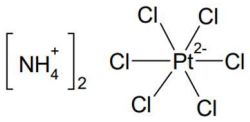
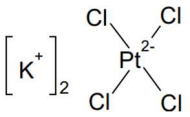
In general, the acute dataset of acute oral toxicity, acute dermal toxicity, skin irritation, eye irritation, and skin sensitisation are available for the dichloride, diacetate, and hydrogen carbonate, while the acute data for the dinitrate are limited to skin and eye irritation studies, with the other acute endpoints filled by read-across. For longer term studies, there are 28-day repeated-dose oral toxicity studies of the diacetate and the hydrogen carbonate, and a reproductive and developmental toxicity screening study for the dinitrate, with the results also used for read-across to other members.

Across these various endpoints classifications have only been required for: Acute Oral Toxicity Cat 4 (diacetate and hydrogen carbonate), Skin Irritation Cat 2 (dichloride), and Eye Irritation (dichloride and diacetate Cat 2, hydrogen carbonate Cat 1). There are also a couple of occupational epidemiology studies supportive of the conclusion that tetraammineplatinum dichloride – and hence also the other tetraammineplatinum substances – do not possess the ability to cause respiratory sensitisation.

The other toxicity endpoint for which data are available is mutagenicity. In vitro testing has shown evidence of genotoxicity of the tetraammineplatinum substances, but an in vivo transgenic rodent assay undertaken as an apical assay was negative and therefore no classification for mutagenicity is applicable.

2.5. Complex halogenated platinum substances (chloroplatinates)

This group comprises hexachloroplatinate in acid form (and hydrate), and as its dipotassium salt and diammonium salt, plus the dipotassium salt of tetrachloroplatinate.

Substance	CAS number	Chemical structure
Hexachloroplatinic acid (and hydrate)	16941-12-1	
Dipotassium hexachloroplatinate	16921-30-5	
Diammonium hexachloroplatinate	16919-58-7	
Dipotassium tetrachloroplatinate	10025-99-7	

All four substances are classified as highly potent respiratory sensitisers (Cat 1A). Across all of the PGM substances covered in this document, these are the only ones classified as respiratory sensitisers. This is based on strong occupational epidemiology evidence supported by laboratory animal study data. All four are also classified for skin sensitisation (Cat 1B).

Aside from sensitisation endpoints, most or all of the substances in the group have also been tested for acute oral toxicity, skin irritation, eye irritation, and genotoxicity, and diammonium hexachloroplatinate has additionally undergone testing in a 28-day repeat-dose oral toxicity study and a reproductive and developmental toxicity screening study.

All four substances in the group are classified as Acute Oral Toxicity Cat 3.

Hexachloroplatinic acid (and hydrate) required classification as Skin Corrosive Cat 1B – and hence automatically also Eye Damage Cat 1. The data for the other three substances also required them to be classified as Eye Damage Cat 1 but indicate they do not require classification for skin irritation. However, dipotassium tetrachloroplatinate is classified as Skin Irritant Cat 2 according to its EU Harmonised Classification.

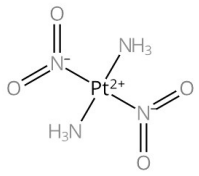
The genotoxicity and reproductive and developmental toxicity screening tests conducted on diammonium hexachloroplatinate showed classifications for those endpoints were not required, but

a classification of STOT-RE 1 was necessary based on effects observed in the kidneys from repeated dosing. The STOT-RE 1 classification was also applied to the other two hexachloroplatinates (the acid and the potassium salt), but not to dipotassium tetrachloroplatinate.

In vivo genotoxicity testing with diammonium hexachloroplatinate and dipotassium tetrachloroplatinate was negative and therefore no classification for mutagenicity was required.

2.6. Other platinum substances – monoconstituent substances

Only one substance with an active EU REACH Registration falls within this group: diammineplatinum (II) nitrite.

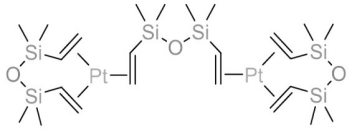
Substance	CAS number	Chemical structure
Diammineplatinum(II) nitrite	14286-02-3	

The toxicity database for this substance is limited to an acute oral toxicity study, a skin irritation study, an eye irritation study, and an in vitro bacterial gene mutation assay that reported no evidence of mutagenicity but was judged unreliable due to major methodological deficiencies. For the other studies, the oral LD_{50} was concluded to be greater than 5,000 mg/kg and there was no irritation observed in the skin irritation study, but the substance did cause moderate irritation in the eye irritation study including sometimes irreversible effects. Consequently, the substance was classified as Eye Damage Cat 1.

2.7. Other platinum substances – UVCBs

The remaining platinum substances not covered by the above groups are four UVCBs: Karstedt concentrate; two substances colloquially known as forms of platinum nitrate; and a substance colloquially known as ‘Pt concentrate P’.

2.7.1. Karstedt concentrate (1,3-diethenyl-1,1,3,3-tetramethyldisiloxane and its platinum(0) complexes)

Substance	CAS number	Chemical structure
1,3-diethenyl-1,1,3,3-tetramethyldisiloxane and its platinum(0) complexes (‘Karstedt concentrate’)	Not specified	

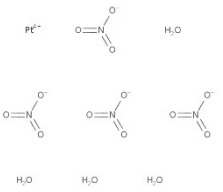
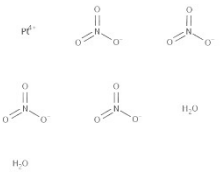
Note: the structures depicted for UVCB substances are for illustration only and do not necessarily represent the real-world ratios of the constituents, nor the dynamic intra- and inter-molecular structural interactions.

Studies of acute oral toxicity, skin irritation, eye irritation, skin sensitisation, and mutagenicity demonstrated corresponding hazard classifications are not required for Karstedt concentrate. In a combined repeated dose toxicity and reproductive and developmental toxicity screening study,

increased post-implantation loss and stillbirths and a consequent reduced live birth index were observed in the mid- and high-dose groups. A follow-up Extended One-Generation Reproductive Toxicity Study (EOGRTS) confirmed the reproductive toxicity potential of Karstedt concentrate and a classification of Reproductive Toxicity Cat 1B was assigned.

2.7.2. 'Platinum nitrates'

This group comprises platinum(IV) aqua hydroxo nitrato complexes (EC 701-319-4) and Platinum (IV) nitrate / nitric acid solution (EC 432-400-1).

Substance	CAS number	Chemical structure
Platinum(IV) aqua hydroxo nitrato complexes	701-319-4	
Platinum (IV) nitrate / nitric acid solution	10102-09-7	

Note: the structures depicted for UVCB substances are for illustration only and do not necessarily represent the real-world ratios of the constituents, nor the dynamic intra- and inter-molecular structural interactions.

Both substances were corrosive to skin, on testing, and classified as Skin Corrosive Cat 1A. Consequently, eye irritation testing was waived and each substance was automatically classified as Eye Damage Cat 1. Acute toxicity testing was also waived, without classifications being assigned, except in the case of an Acute Inhalation Toxicity Cat 3 classification assigned to platinum (IV) nitrate / nitric acid solution based on read-across of data for nitric acid.

Platinum(IV) aqua hydroxo nitrato complexes is not classified for skin sensitisation, while Platinum (IV) nitrate / nitric acid solution is classified as Skin Sensitisation 1B. The sensitisation data supporting the former is a guinea pig maximisation test which was negative (non-sensitising), while the latter relies on the same test and in addition a non-standard local lymph node assay of questionable reliability which was positive (sensitising). Platinum(IV) aqua hydroxo nitrato complexes was also applied with the supplementary EUH071 code for potential corrosion to the respiratory tract following inhalation.

Classifications have not been required for mutagenicity, target organ toxicity, or reproductive and developmental toxicity. Although evidence of genotoxicity was found in an in vitro bacterial reverse mutation assay and an in vitro mammalian cell gene mutation assay that was used to support dossier registrations for both substances, a subsequent in vivo combined comet/micronucleus test of EC 701-319-4 found no biologically relevant genotoxic responses.

A combined repeated dose toxicity and reproductive and developmental toxicity screening study on EC 701-319-4 has been undertaken and does not result in classification.

2.7.3. Pt concentrate P (Phosphato, nitrito, sulfato, amino, aquo platinate (II) complex)

Substance	CAS number	Chemical structure
Phosphato, nitrito, sulfato, amino, aquo platinate (II) complex (Pt concentrate P)	Not specified	Not specified

Note: the structures depicted for UVCB substances are for illustration only and do not necessarily represent the real-world ratios of the constituents, nor the dynamic intra- and inter-molecular structural interactions.

Pt concentrate P was found to be damaging to skin, requiring classification as Skin Corrosive Cat 1B. Consequently, testing for eye irritation was waived and a classification of Eye Damage Cat 1 was automatically assigned. Testing for acute toxicity and for skin sensitisation was also waived without classifications assigned. The only other data available for this substance are from genotoxicity studies. Pt concentrate P was considered to be mutagenic in an in vitro bacterial reverse mutation assay, but was negative in an in vitro micronucleus test. A weight of evidence was used to conclude the substance does not require classification for mutagenicity based on data for various other platinum substances and a study showing that, in simulated gastric fluid, Pt concentrate P reacts to Pt(IV).

Table 1: Human health hazard classification and toxicity data overview of the Platinum substances

		CAS number EC number	Acute toxicity			Irritation		Sensitisation		Mutagenicity	Cancer effects	Target organ effects	Repro/ dev effects
			Oral	Dermal	Inhalation	Skin	Eye	Skin	Respiratory				
Elemental platinum and platinum oxides													
Platinum		7440-06-4 231-116-1	D	W	W	PD & RA	PD & RA	RA	ND	D [a]	ND	PD & RA	PD & RA
Platinum oxide		12035-82-4 234-831-7	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Platinum dioxide (and hydrate)		1314-15-4 215-223-0	D	ND	ND	D	D	D	ND	PD & RA [a]	ND	D	ND
Hexahydroxyplatinum substances													
Dihydrogen hexahydroxyplatinate		51850-20-5 257-471-2	D	ND	ND	D	D **Cat 2**	D	ND	PD & RA [b]	ND	D	D
Dihydrogen hexahydroxyplatinate, compound with 2-aminoethanol (1:2)		68133-90-4 268-717-3	D	ND	ND	D **Cat 1B**	W **Cat 1** [c]	D	ND	D	ND	D	D
Tetraammine Platinum **substances**													
Tetraammine platinum dichloride		13933-32-9 237-706-5	D	D	ND	D **Cat 2**	D **Cat 2**	D	PD [d]	[e]	ND	PD	RA
Tetraammine platinum (II) diacetate		[*not specified*] 457-310-8	D **Cat 4**	D	ND	D	D **Cat 2**	D	ND	[e]	ND	D	RA
Tetraammine platinum dinitrate		20634-12-2 243-929-9	RA	RA	ND	D	D	RA	ND	[e]	ND	PD & RA	D
Tetraammine platinum (II) hydrogen carbonate		123439-82-7 426-730-3	D **Cat 4**	D	ND	D	D **Cat 1**	D	ND	[e]	ND	D	RA
Complex halogenated platinum substances (chloroplatinates)													
Hexachloroplatinic acid (and hydrate) [f]		16941-12-1 241-010-7	D **Cat 3**	ND	ND	D **Cat 1B**	W **Cat 1**	D **Cat 1B**	D **Cat 1A**	RA	ND	RA **STOT-RE 1**[g]	RA
Dipotassium hexachloroplatinate [f]		16921-30-5 240-979-3	D **Cat 3**	ND	ND	RA	D **Cat 1**	D **Cat 1B**	D **Cat 1A**	RA	ND	RA **STOT-RE 1**[g]	RA
Diammonium hexachloroplatinate [f]		16919-58-7 240-973-0	D **Cat 3**	ND	ND	D	D **Cat 1**	D **Cat 1B**	D **Cat 1A**	D	ND	D **STOT-RE 1**[g]	D
Dipotassium tetrachloroplatinate [f]		10025-99-7 233-050-9	D **Cat 3**	ND	ND	**Cat 2** [h]	D **Cat 1**	RA **Cat 1B**	D **Cat 1A**	D	ND	RA	RA
Other platinum substances – monoconstituent substances													
Diammineplatinum(II) nitrite		14286-02-3 238-203-3	D	ND	ND	D	D **Cat 1**	ND	ND	PD	ND	PD	ND
Other platinum substances – substances of unknown or variable composition or of biological origin (UVCB)													
Platinum nitrate	Platinum(IV) aqua hydroxo nitrato complexes	[*not specified*] 701-319-4	W [i]	W [i]	W [l] Irritating	D **Cat 1A**	W [i] **Cat 1**	D	ND	D [j]	ND	D [k]	D[k]
	Platinum (IV) nitrate / nitric acid solution	10102-09-7 432-400-1	W [i]	W [i]	W [l] **Cat 3**	D **Cat 1A**	W [i] **Cat 1**	D **Cat 1B**	ND	PD [m]	ND	D	D
Phosphato, nitrito, sulfato, amino, aquo platinate (II) complex (Pt concentrate P)		[*not specified*] 955-621-8	W [i]	W [i]	W [i]	D **Cat 1B**	W [i] **Cat 1**	W [i]	ND	PD & RA [n]	ND	ND	ND
1,3-diethenyl-1,1,3,3-tetramethyldisiloxane and its platinum(0) complexes (Karstedt concentrate)		[*not specified*] 701-315-2	D	ND	ND	D	D	D	ND	D	ND	D	D **Repro 1B**

D	**Classification not required**: Data available (D).
PD/RA	**Classification not required**: Partial data available (PD), read-across (RA), partial data and read-across (PD & RA), or read-across of partial data (RA PD).
ND/W	**Classification not required**: No data available (ND) and/or data requirement waived (W).
ND/W	**Classified based on assumed hazard**: No data available (ND) and/or data requirement waived (W).
PD/RA	**Classified**: Partial data available (PD), read-across (RA), partial data and read-across (PD & RA), or read-across of partial data (RA PD).
D	**Classified**: Data available (D).

[a] The limited genotoxicity data for platinum dioxide are considered unreliable. Additional genotoxicity testing of various platinum compounds have been conducted to clarify their genotoxic potential. Genotoxicity testing on platinum powder consisted of negative mammalian cell gene mutation assay, negative in-vitro micronucleus assay and a positive (TA98 & TA100, -S9) Ames assay.

[b] There was evidence of in vitro genotoxicity of dihydrogen hexahydroxyplatinate but not in an in vivo combined comet/micronucleus assay with the read-across substance dihydrogen hexahydroxyplatinate, compound with 2-aminoethanol. Additional genotoxicity testing of various platinum compounds has also been completed and supports a lack of mutagenic classification.

[c] The result of the in vitro bovine corneal opacity study with dihydrogen hexahydroxyplatinate, compound with 2-aminoethanol did not enable classification for eye damage/irritation, but the classification as a Cat 1B skin corrosive means eye damage is implicit and classification as Eye damage Cat 1 is assigned.

[d] Two occupational epidemiology studies are available that do not indicate tetraammineplatinum dichloride possesses the potential to cause respiratory sensitisation.

[e] In vitro testing has shown evidence of genotoxicity of the tetraammineplatinum substances; initial in vivo testing of tetraammineplatinum dichloride was equivocal. Classification for mutagenicity is not currently required, but further confirmatory in vivo testing is planned.

[f] The hazard classifications listed for the chloroplatinates are the 'self classifications' assigned by industry that go beyond the harmonized classifications for these substances.

[g] The target organ was kidney.

[h] The available data indicate classification for skin irritation is not required for dipotassium tetrachloroplatinate. However, there is an EU harmonized classification of Skin Irritant Category 2 for this substance.

[i] Waived due to substance corrosivity.

[j] In vitro testing has shown evidence of genotoxicity. In vivo testing in a combined comet and micronucleus assay was negative.

[k] Data for dihydrogen hexahydroxyplatinate were used for read-across. The hazard classification will be reviewed once substance-specific data (OECD 422 repro-dev screening study) are available.

[l] No inhalation toxicity data are available and acute toxicity testing was waived due to the corrosivity of the substance. Read-across data for nitric acid were used for the acute inhalation toxicity hazard classification.

[m] In vitro testing has shown evidence of genotoxicity. Classification for mutagenicity is not currently required, but confirmatory in vivo testing is planned.

[n] Phosphato, nitrito, sulfato, amino, aquo platinate (II) complex has itself been tested for genotoxicity only in an in vitro bacterial reverse mutation assay and an in vitro micronucleus assay. In the bacterial assay, there was clear evidence of mutagenicity in three of the five strains tested, while in the micronucleus study the substance was found to be non-clastogenic and non-aneugenic. In vivo genotoxiciy (comet and micronuclues) studies for other platinum substances including ammonium hexachloroplatinate, hexahydroxyplatinic acid, and tetraaammineplatinum dichloride are additionally used in a weight of evidence, alongside bioaccessibility data showing the substance reacts to Pt(IV) in simulted gastric fluid, to conclude the substance does not require classification for mutagenicity.

3. Palladium compounds

3.1. Introduction and summary

Active EU REACH Registration dossiers for 18 palladium substances were identified. A further two palladium substances (diammonium hexachloropalladate and Tetrakis(triphenylphosphine) palladium) with inactive dossiers due to cessation of manufacture have been included as they are similar to other palladium substances with active registrations and they have toxicity testing data helpful in providing understanding of the hazard profile of these types of palladium substances. An overview of the human health hazard classifications and toxicity data for these 20 substances is provided in Table 2. For this purpose, the substances have been grouped as follows:

- Elemental palladium and simple insoluble palladium substances
- Soluble/hydrolysable ionic palladium salt substances
- Tetraamminepalladium substances
- Complex halogenated palladium substances
- Other specific palladium substances

Aside from the first group (elemental Pd and simple insoluble Pd substances), most palladium substances tested have shown to be Cat 4 acute oral toxicants, Cat 1 or 2 eye irritants, and skin sensitisers. A minority are also skin irritants, with the acidic palladium sulphate, palladium dinitrate, and dihydrogen tetrachloropalladate requiring a Skin Corrosive Cat 1 classification, and the dipotassium and diammonium hexachloropalladates requiring a Skin Irritation Cat 2 classification. Studies of acute dermal toxicity, mutagenicity, and reproductive and developmental screening, which are variously available for one or more palladium substances across the different groups, have almost universally been unremarkable and not required classification. The main exception to this is the classification of STOT-RE 2 for tetraammine palladium (II) hydrogen carbonate based on effects on the stomach and/or spleen. Such classification was not required for tetraamminepalladium dichloride, the only other substance in this group with repeated-dose toxicity data, and the remaining tetraamminepalladium substances in this group have also not been classified for target organ effects.

3.2. Elemental palladium and simple insoluble palladium substances

The elemental palladium and simple insoluble palladium substances group comprises elemental palladium, palladium monoxide, and palladium dihydroxide.

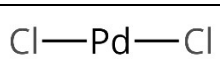
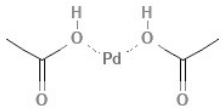
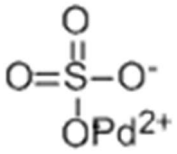
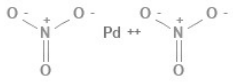
Substance	CAS number	Chemical structure
Palladium	7440-05-3	Pd
Palladium monoxide	1314-08-5	O=Pd
Palladium dihydroxide	12135-22-7	HO—Pd—OH

These forms of palladium are considered to be largely inert. Across these three substances, only one hazard classification has been assigned: an Eye Irritation Cat 2 for palladium dihydroxide. The three substances can be considered as a read-across group and results for one substance have been

applied to another substance for various endpoints, especially for elemental palladium for which skin sensitisation and skin irritation / corrosion data are directly available. In addition, a repeated dose toxicity and reproductive and developmental screening study (OECD 422) is available on palladium dihydroxide. Collectively across the group, though, there are acute oral toxicity, skin irritation, eye irritation, skin sensitisation, mutagenicity, and screening reproductive and developmental toxicity studies.

3.3. Soluble/hydrolysable ionic palladium salt substances

This group comprises the inorganic salts palladium dichloride, palladium sulphate, and palladium dinitrate (UVCB), and the simple organic salt palladium (II) acetate.

Substance	CAS number	Chemical structure
Palladium dichloride	7647-10-1	
Palladium (II) acetate	3375-31-3	
Palladium sulphate	13566-03-5	
Palladium dinitrate	10102-05-3	

Note: the structures depicted for UVCB substances are for illustration only and do not necessarily represent the real-world ratios of the constituents, nor the dynamic intra- and inter-molecular structural interactions.

Across the group, there are studies of acute oral toxicity, skin irritation, eye irritation, skin sensitisation, mutagenicity, and repeated dose toxicity. In the main, each substance has itself been tested in each of those study types, aside from when studies of eye irritation and, in one case, skin sensitisation have been waived based on skin corrosivity. No data on reproductive and developmental toxicity are available for any of these palladium substances, but for palladium dichloride and palladium dinitrate a combined repeated dose toxicity / reproductive and developmental screening study of palladium hydroxide is used for read-across.

Each of the four substances has low acute oral toxicity, with palladium (II) acetate not requiring classification and the other three substances classified as Cat 4.

Palladium sulphate and palladium dinitrate, which produce acidic solutions in water, were corrosive and classified as Skin Corrosive Cat 1B. Consequently, eye irritation testing for these two substances was waived and they were automatically classified as Eye Damage Cat 1. Skin sensitisation was also waived for palladium sulphate due to its corrosivity, and no classification was assigned, while palladium dinitrate was tested and found to be non-sensitising.

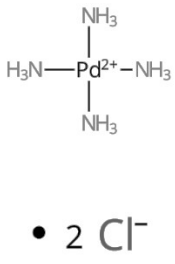
Palladium dichloride and palladium (II) acetate were not irritating to skin, but testing for eye irritation showed they required classification as Eye Damage Cat 1. Both substances also showed evidence of skin sensitisation on testing and were classified as Skin Sensitisation Cat 1.

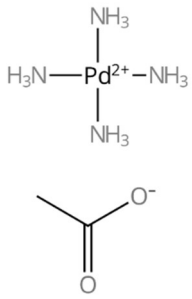
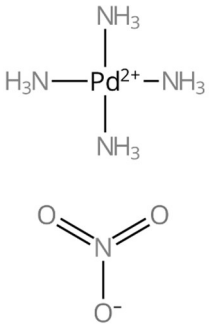
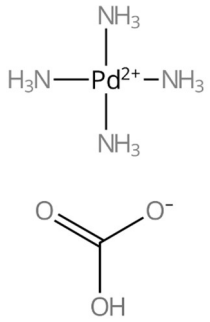
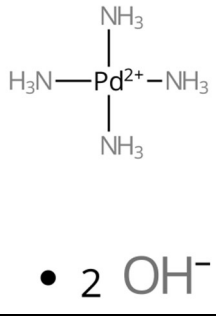
Batteries of genotoxicity tests for palladium dichloride and palladium dinitrate showed them to be non-mutagenic, and similarly the more limited testing of palladium acetate and palladium sulphate did not indicate they are mutagens.

The combined repeated dose oral toxicity and reproductive and developmental toxicity screening study for palladium hydroxide used for read-across indicates non-classification for these substances.

3.4. Tetraamminepalladium substances

The tetraamminepalladium substances group comprises five salts of tetraamminepalladium: the dichloride, diacetate, dinitrate, hydrogen carbonate, and dihydroxide. All are monoconstituent substances and highly soluble in water; though, the dihydroxide was additionally found to be unstable in water. Tetraamminepalladium dinitrate is stated to only be available in solution form due to the explosive properties of the solid form.

Substance	CAS number	Chemical structure
Tetraamminepalladium (II) dichloride	13815-17-3	

Tetraamminepalladium (II) diacetate	61495-96-3	
Tetraamminepalladium (II) dinitrate	13601-08-6	
Tetraamminepalladium (II) hydrogen carbonate	134620-00-1	
Tetraamminepalladium (II) dihydroxide	68413-68-3	

Toxicity data are predominantly available for the hydrogen carbonate and dichloride salts, and these data have been read-across to the other tetraamminepalladium salts. Collectively, these include studies of acute oral toxicity, acute dermal toxicity, skin irritation, eye irritation, skin sensitisation, screening level repeated dose and reproductive and developmental toxicity, and mutagenicity.[2]

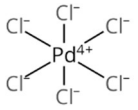
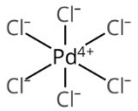
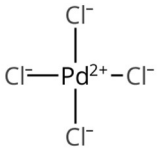
[2] One or more genotoxicity studies are available for three substances in the tetraamminepalladium group: hydrogen carbonate (in vitro bacterial mutagenicity, in vitro chromosome aberration, in vivo miconucleus); dichloride (partial in vitro bacterial mutagenicity, partial in vitro micronucleus); and acetate (in vitro mammalian cell gene mutation).

The data have prompted the substances to be classified for Acute Oral Toxicity (Cat 4), Eye Irritation (mostly Cat 2),[3] and Skin Sensitisation (Cat 1A). Classifications were not required for acute dermal toxicity, skin irritation, mutagenicity, or reproductive and developmental toxicity.

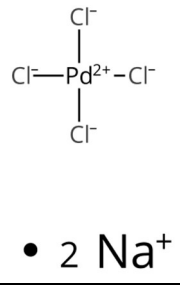
Tetraamminepalladium hydrogen carbonate additionally has a harmonised classification of STOT-RE 2. The harmonized classification states the STOT-RE classification is based on effects on the stomach. The self-classification of this substance in the REACH Registration dossier also includes a classification of STOT-RE but based on effects on the spleen observed in a 28-day repeated dose oral toxicity study. The dossier author states that the "*observed effects on the stomach are likely the result of local irritancy*". None of the other REACH-Registered tetraamminepalladium substances has undergone 28-day oral toxicity testing, but such target organ effects were not observed in a reproductive and developmental toxicity screening study of tetraamminepalladium dichloride, and none of the other REACH-Registered tetraamminepalladium substances has a STOT-RE classification.

3.5. Complex halogenated palladium substances

The complex halogenated palladium substances group comprises the disodium and dihydrogen tetrachloropalladates, and the dipotassium and diammonium hexachloropalladates.

Substance	CAS number	Chemical structure
Dipotassium hexachloropalladate	16919-73-6	 • 2 K^+
Diammonium hexachloropalladate	19168-23-1	 • 2 NH_4^+
Dihydrogen tetrachloropalladate	16970-55-1	 • 2 H^+

[3] Tetraammine palladium hydrogen carbonate has a more severe classification of Eye Damage Cat 1, based on limited data that do not permit a definitive classification and the expectation that the effects observed would be irreversible.

Disodium tetrachloropalladate	13820-53-6	

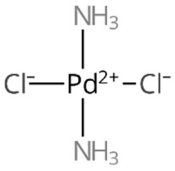
There are studies of acute oral toxicity, skin irritation, eye irritation, and skin sensitisation for most of the four substances, plus genotoxicity studies and a repeated dose toxicity and reproductive and developmental toxicity screening study for one hexachloropalladate and one tetrachloropalladate.

The general profile of the halogenopalladates supported by those studies is Acute Oral Toxicity (Cat 4), Eye Damage (Cat 1), Skin Sensitisation (Cat 1A or 1B), and a variable potential for skin irritation with the acidic dihydrogen tetrachloropalladate a Skin Corrosive Cat 1A, the two hexachloropalladates Skin Irritant Cat 2, and the disodium tetrachloropalladate not a skin irritant. None of the four halogenopalladates are classified for mutagenicity, reproductive/developmental toxicity, or target organ toxicity, based on the corresponding data available, and there are no data available on acute dermal or inhalation toxicity, respiratory sensitisation, or carcinogenicity.

3.6. Other specific palladium substances

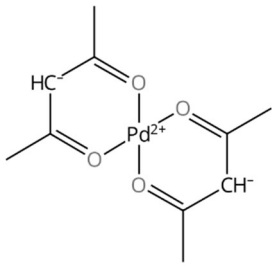
The other specific palladium substances group comprises diamminedichloropalladium, palladium (II) di(4-oxopent-2-en-oate), and two triphenylphosphine palladium compounds.

3.6.1. Diamminedichloropalladium

Substance	**CAS number**	**Chemical structure**
Diamminedichloro palladium	14323-43-4	

Diamminedichloropalladium has been tested in acute oral toxicity, acute dermal toxicity, skin irritation, eye irritation, skin sensitisation, mutagenicity, and repeated dose general toxicity and reproductive and developmental toxicity (screening) studies. These showed it to cause serious Eye Damage (Cat 1) and to require classification for Acute Oral Toxicity (Cat 4). No other hazard classifications were required.

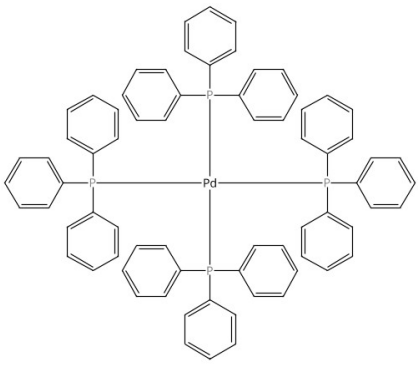
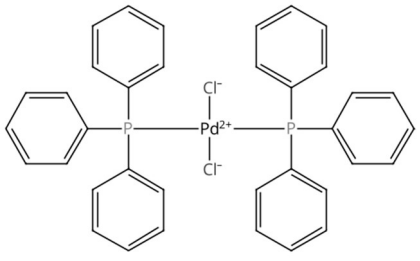
3.6.2. Palladium (II) di(4-oxopent-2-en-oate)

Substance	CAS number	Chemical structure
Palladium (II) di(4-oxopen-2-en-oate)	14024-61-4	

Palladium (II) di(4-oxopent-2-en-oate) is an ionic organic Pd salt with a much lower water solubility than those substances of the 'Soluble/hydrolysable ionic Pd salt substances' group (reported water solubility of 0.011 g/L).

Like diamminedichloropalladium, it has been tested in acute oral toxicity, acute dermal toxicity, skin irritation, eye irritation, skin sensitisation, mutagenicity, and repeated dose general toxicity and reproductive and developmental toxicity (screening) studies. These showed it to cause serious Eye Damage (Cat 1) and to also require classification for Acute Oral Toxicity (Cat 4), and also Skin Sensitisation Cat 1A based on the results of a preliminary skin sensitisation test in which it showed evidence of being a strong sensitiser. No other hazard classifications were required.

3.6.3. Triphenylphosphine palladium compounds

Substance	CAS number	Chemical structure
Tetrakis(triphenylphoshine) palladium	14221-01-3	
Dichlorobis(triphenylphoshine) palladium	13965-03-2	

The two triphenylphosphine palladium compounds are tetrakis(triphenylphoshine) palladium, and dichlorobis(triphenylphoshine) palladium. Both are very poorly soluble in water (0.00012 and <0.00001 g/L, respectively). There are no toxicity data for dichlorobis(triphenylphosphine)

palladium, and only studies of skin irritation and eye irritation are available for tetrakis(triphenylphospine) palladium. These studies showed the substance to not be a skin or eye irritant.

Table 2: Human health hazard classification and toxicity data overview of the Palladium substances

	CAS number EC number	Acute toxicity			Irritation		Sensitisation		Mutagenicity	Cancer effects	Target organ effects	Repro/ dev effects
		Oral	Dermal	Inhalation	Skin	Eye	Skin	Respiratory				
Elemental palladium and simple insoluble palladium substances												
Palladium	7440-05-3 231-115-6	RA	W	W	RA	RA	D	ND	D	ND	RA	RA PD
Palladium monoxide	1314-08-5 215-218-3	D	ND	ND	D	D	RA	ND	PD & RA	ND	RA	RA PD [a]
Palladium dihydroxide	12135-22-7 235-219-2	RA	W	W	D	PD & RA **Cat 2**	D	ND	D	ND	RA	D
Soluble/hydrolysable ionic palladium salt substances												
Palladium dichloride	7647-10-1 231-596-2	D **Cat 4**	ND	ND	D	D **Cat 1**	D **Cat 1**	ND	D	ND	RA	RA [b]
Palladium (II) acetate	3375-31-3 222-164-4	D	ND	ND	D	D **Cat 1**	D **Cat 1**	ND	PD	ND	PD	ND
Palladium sulphate	13566-03-5 236-957-8	D **Cat 4**	ND	ND	D **Cat 1B**	W **Cat 1**	W	ND	PD	ND	PD	ND
Palladium dinitrate	10102-05-3 233-265-8	D **Cat 4**	ND	ND	D **Cat 1B**	W **Cat 1**	D	ND	D	ND	PD	RA [b]
Tetraamminepalladium substances												
Tetraamminepalladium (II) dichloride	13815-17-3 237-489-7	RA **Cat 4**	RA	ND	D	D **Cat 2**	D **Cat 1A**	ND	PD & RA	ND	PD & RA	RA
Tetraamminepalladium (II) diacetate	61495-96-3 262-819-1	RA **Cat 4**	RA	ND	RA	RA **Cat 2** [c]	RA **Cat 1A**	ND	PD & RA	ND	RA [d]	RA PD
Tetraamminepalladium (II) dinitrate	13601-08-6 237-078-2	RA **Cat 4**	ND [e]	ND	RA	RA **Cat 2**	PD & RA **Cat 1A**	ND	RA	ND	RA [e]	RA [e]
Tetraamminepalladium (II) hydrogen carbonate	134620-00-1 425-270-0	D **Cat 4**	D	ND	D	D **Cat 1**	D **Cat 1A**	ND	PD & RA	ND	D **STOT-RE 2** [f]	RA PD
Tetraamminepalladium (II) dihydroxide	68413-68-3 270-241-6	RA **Cat 4**	ND [g]	ND	RA	RA **Cat 2**	RA **Cat 1A**	ND	RA	ND	ND [e]	ND [e]
Complex halogenated palladium substances												
Dipotassium hexachloropalladate	16919-73-6 240-974-6	D **Cat 4**	ND	ND	D **Cat 2**	D **Cat 1**	RA **Cat 1B**	ND	PD & RA	ND	RA	RA PD
Diammonium hexachloropalladate	19168-23-1 242-854-9	D **Cat 4**	ND	ND	D **Cat 2**	D **Cat 1**	D **Cat 1B**	ND	D	ND	D	PD
Dihydrogen tetrachloropalladate	16970-55-1 241-047-9	D **Cat 4**	ND	ND	D **Cat 1A**	W **Cat 1**	D **Cat 1A**	ND	D	ND	PD & RA	RA PD
Disodium tetrachloropalladate	13820-53-6 237-502-6	D **Cat 4**	ND	ND	D	D **Cat 1**	D **Cat 1A**	ND	RA	ND	D	D
Other specific palladium substances												
Diamminedichloro palladium	14323-43-4 238-269-3	D **Cat 4**	D	ND	D	D **Cat 1**	D	ND	D	ND	D	D
Tetrakis(triphenylphosphine) palladium	14221-01-3 238-086-9	ND	ND	ND	D	D	ND	ND	ND	ND	ND	ND
Dichlorobis(triphenylphosphine) palladium	13965-03-2 237-744-2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

Palladium (II) di(4-oxopent-2-en-2-oate	14024-61-4 237-859-8	D **Cat 4**	D	ND	D	D **Cat 1**	D **Cat 1A** [h]	ND	D	ND	D	D

D **Classification not required**: Data available (D).

RA/PD **Classification not required**: Partial data available (PD), read-across (RA), partial data and read-across (PD & RA), or read-across of partial data (RA PD).

ND/W **Classification not required**: No data available (ND) and/or data requirement waived (W).

ND/W **Classified based on assumed hazard**: No data available (ND) and/or data requirement waived (W).

RA/PD **Classified**: Partial data available (PD), read-across (RA), partial data and read-across (PD & RA), or read-across of partial data (RA PD).

D **Classified**: Data available (D).

[a] No explanation is provided in the dossier for the absence of classification for reproductive toxicity beyond "data lacking". However, for other hazard classification endpoints, the dossier refers to this substance (palladium monoxide) being part of a read-across group with palladium and palladium hydroxide. Since a reproductive and developmental toxicity screening study (OECD 422) is available for palladium hydroxide, it is assumed that this also contributed to the conclusion that no classification for reproductive toxicity is required for palladium monoxide.

[b] Read-across to palladium hydroxide (additional data generation planned in 2026).

[c] The substance was found to be non-irritating in an in vitro study (isolated chicken eyes) but was classified as a Cat 2 eye irritant based on in vivo eye irritation studies with the tetraammine palladium dichloride and with tetraammine palladium hydrogen carbonate.

[d] STOT-RE is read-across to tetraamminepalladium dichloride.

[e] The dossier states 'data lacking' but it is believed this endpoint can be read-across to tetraamminepalladium dichloride.

[f] The harmonized classification states the STOT-RE classification is based on effects on the stomach. The self-classification of this substance in the dossier states the STOT-RE classification is based on effects on the spleen. The dossier author states that the "observed effects on the stomach are likely the result of local irritancy".

[g] The dossier states 'data lacking' but it is believed this endpoint can be read-across to tetraamminepalladium hydrogen carbonate.

[h] The data do not allow distinction between Cat 1A and Cat 1B; therefore, Cat 1A was assigned on a precautionary basis.

Source: REACH disseminated dossiers available on the ECHA webpage: https://echa.europa.eu/fr/home (date of the consultation: 07/02/2024)

4. Rhodium compounds

4.1. Introduction and summary

Active EU REACH Registration dossiers for 13 rhodium substances were identified. A further four rhodium substances (rhodium (III) acetate; triammonium hexachlororhodate; carbonylhydrotris(triphenylphosphine)rhodium; and diammonium sodium hexakis(nitrito-N)rhodate)) that have inactive registrations have been included as they are similar to other rhodium substances with active registrations and/or they have toxicity testing data helpful in providing understanding of the hazard profile of these types of rhodium substance.

An overview of the human health hazard classifications and toxicity data for these 17 substances is provided in Table 3. They are divided into the following groups:

- Elemental Rh and simple insoluble rhodium substances
- Poorly soluble inorganic Rh(III) substances
- Soluble inorganic Rh (III) substances, other than chlororhodate substances
- Complex halogenated rhodium substances
- Triphenylphosphine rhodium substances.
- Other specific rhodium substances

Unlike chloroplatinates, the main hazard of rhodium compounds is not respiratory sensitisation. Cases of respiratory sensitisation due to industrial exposures to rhodium compounds are relatively rare and in some instances may reflect cross-sensitisation reactions to chloroplatinates.

Some rhodium(I) and rhodium(III) compounds have tested positive in assays for delayed skin contact hypersensitivity potential.

The majority of rhodium compounds possess only low to moderate acute toxicity. Local eye and skin effects are typified by a spectrum of low to moderate contact irritancy except for the corrosivity evident for compounds with a very low pH, such as some inorganic rhodium(III) compounds.

Although there have been occasional reports of target organ toxicity or reproductive toxicity in animal studies, evidence from recent repeat-dose toxicity studies in rodents conducted in accordance with Good Laboratory Practice (GLP) and modern test guidelines suggest that even bioavailable rhodium compounds possess limited systemic toxicity at doses relevant to occupational contexts.

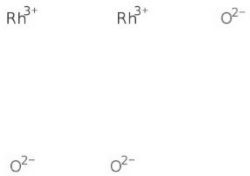
The more soluble Rhodium(III) compounds have been shown to be genotoxic in short-term in vitro assays and in some in vivo tests, including consistent positive results for various soluble rhodium(III) compounds in bacterial mutagenicity tests. Therefore, they were classified as Mutagen Category 2 through self-classification as a precautionary measure. More recent genotoxicity data has been or is in the process of being generated to more definitively address the genotoxic hazard (e.g., rhodium trisulphate is no longer classified as mutagenic based on more recent GLP and guideline compliant in-vivo genotoxicity data).

Overall, the data sets of acute toxicity of rhodium compounds do not indicate significant concern with the exception of some specific cases where category 3 and 4 classifications have been designated. The main concerns are for a few soluble inorganic Rh(III) compounds, and their potential for genotoxicity. Historically there has been a lack of data on chronic and

reproductive/developmental toxicity, although data have recently been generated for Rh trichloride and Rh trinitrate, for example, in GLP and guideline compliant assays.

4.2. Elemental Rh and simple insoluble Rh substances

Rhodium, dirhodium trioxide, and rhodium trihydroxide are a group of insoluble compounds that are considered inert.

Substance	CAS number	Chemical structure
Rhodium	7440-16-6	
Dirhodium trioxide	12036-35-0	
Rhodium trihydroxide	21656-02-0	

Toxicity data are only available for dirhodium trioxide and rhodium trihydroxide. The available data, including studies of acute oral toxicity, skin irritation, eye irritation, skin sensitisation, and genotoxicity suggest that this group of rhodium substances is not expected to have any significant effects on human health and no hazard classifications have been assigned to these substances.

4.3. Poorly soluble inorganic Rh (III) substances

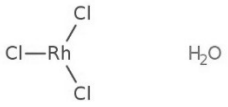
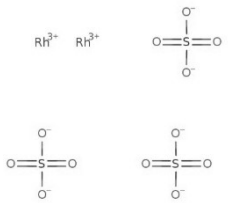
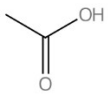
There is only one member of this group: rhodium triiodide.

Substance	CAS number	Chemical structure
Rhodium triiodide	15492-38-3	

This substance has no toxicity data besides an in vitro bacterial mutagenicity study that showed evidence of mutagenic activity but that used DMSO as a solvent vehicle, which is inappropriate as it is likely to have complexed with the test material. An Ames test conducted with water as the solvent yielded negative results.

4.4. Soluble inorganic rhodium(III) substances other than chlororhodates

The group of soluble inorganic trivalent rhodium compounds includes rhodium trichloride, dirhodium trisulphate, rhodium trinitrate (UVCB), and rhodium acetate (UVCB).

Substance	CAS number	Chemical structure
Rhodium chloride ($RhCl_3$) hydrate / Rhodium trichloride	20765-98-4	
Dirhodium trisulphate	10489-46-0	
Rhodium trinitrate	10139-58-9	 • 1/3 Rh(III)
Rhodium acetate	42204-14-8	 • x Rh(x)

Note: the structures depicted for UVCB substances are for illustration only and do not necessarily represent the real-world ratios of the constituents, nor the dynamic intra and inter-molecular structural interactions.

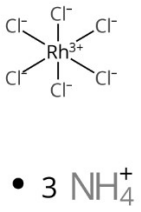
The ability of these substances to dissolve in water affects their toxicity. Upon dissolution in water, dirhodium trisulphate forms a neutral or slightly basic solution. In contrast, rhodium trichloride and trinitrate are both acidic compounds that, upon dissolution in water, release hydrogen ions leading to the formation of acidic solutions. Therefore, rhodium trichloride and trinitrate have higher potential to cause pH related tissue damage. Rhodium trinitrate and rhodium sulphate are classified as Skin Irritant Cat 1B and automatically also therefore Eye Damage Cat 1; whereas rhodium trichloride is classified as skin irritant Cat 2 and eye damage Cat 1 and rhodium acetate is non-irritating to skin but irritant to eyes.

Rhodium trinitrate has been tested for skin sensitisation and is classified as Skin Sensitiser Cat 1A. Rhodium trichloride has also been tested for skin sensitisation and is classified as Skin Sensitiser Cat 1.

Additionally, these rhodium compounds have been found to express mutagenic properties in some studies. Newer in vivo mutagenicity data have recently been generated for dirhodium trisulphate which were negative and so this substance is not classified for mutagenicity, while the other three compounds in this group currently continue to be classified as mutagenic category 2.

4.5. Complex halogenated rhodium substances

There is only one substance in this group: triammonium hexachlororhodate.

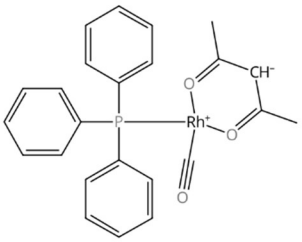
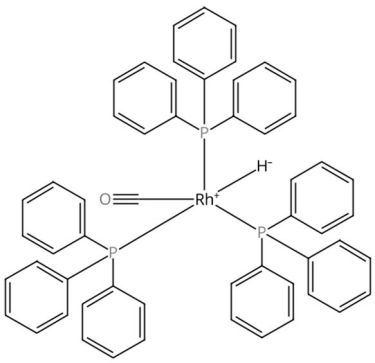
Substance	CAS number	Chemical structure
Triammonium hexachlororhodate	15336-18-2	

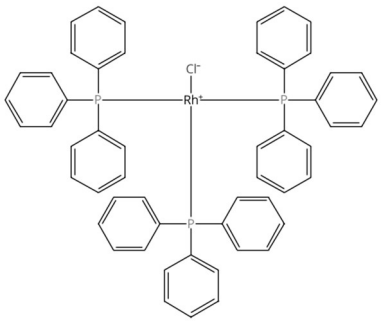
Toxicity data for this substance are limited to an acute oral toxicity study, skin and eye irritation studies, and two limited in vitro bacterial mutagenicity studies.

Toxicity and mortality were observed in the acute oral toxicity study but the LD50 was calculated to be above the 2,000 mg/kg threshold and so classification was not required. There was no evidence of irritation to the skin, while in the eye irritation study severe irreversible effects were observed and the substance was classified as Eye Damage Cat 1. Evidence of genotoxicity in two in vitro bacterial tests, alongside more broad evidence of the genotoxicity of soluble Rh (III) substances meant the substance was classified as Mutagen Cat 2.

4.6. Triphenylphosphine rhodium compounds

This group consists of three rhodium(I) compounds that each form a complex with one or more triphenylphosphine ligands.

Substance	CAS number	Chemical structure
Carbonyl(pentane-2,4-dionato-O,O')(triphenylphosphine)rhodium	25470-96-6	
Carbonylhydrotris(triphenylphosphine)rhodium	17185-29-4	

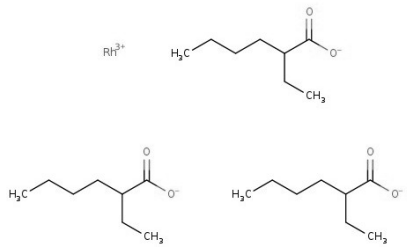
Tris(triphenylphosphine) rhodium (I) chloride	14694-95-2	

The toxicological data set for these compounds is relatively poor, focusing on acute and local toxicity endpoints including skin and eye irritation and skin sensitization, and limited (in vitro bacterial) mutagenicity data.

Overall, these compounds have exhibited a low toxicity profile in the studies that have been performed, which is supported by their insolubility in water and chemical stability under normal conditions of temperature and humidity. Two of the substances were experimentally determined to be non-mutagenic in bacterial mutagenicity studies, and a connection to the genotoxic effects of the soluble inorganic Rh(III) substances is not expected, since the triphenylphosphine compounds group differs both in oxidation state of the metal and in the coordination chemistry of the ligands. No hazard classifications are assigned to any of the three substances.

4.7. Other specific rhodium compounds

4.7.1. Rhodium tris(2-ethylhexanoate)

Substance	**CAS number**	**Chemical structure**
Rhodium tris(2-ethylhexanoate)	20845-92-5	

This substance is an inorganic compound that falls in the EU under the legal definition of a metal salt of 2-ethyl hexanoic acid. Therefore, in the EU the harmonized classification of '2-ethylhexanoic acid and its salts' with a single classification of Repro 1B H360D (under the 18th ATP) applies to this substance. The driver for this hazardous property is hence the organic moiety of the substance.

Aside from the harmonized classification for reprotoxicity, rhodium tris(2-ethylhexanoate) has a very limited toxicity data set, in part due to its corrosive properties. Because of the classification as Skin Corrosive Cat 1B, and Eye Damage Cat 1, no more in vivo testing was performed to assess acute toxicity and no corresponding hazard classifications were assigned.

This substance is insoluble in water and aqueous media. In vitro tests performed at the highest possible concentration of the substance in solvent solution did not indicate any genotoxicity in bacteria, and the substance is not classified for mutagenicity. Other genotoxicity studies have not

been investigated; however, there is a clear difference in chemistry and overall toxicity profile compared to the soluble inorganic rhodium(III) substances group.

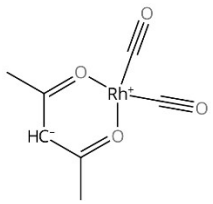
No substance specific data exist for higher tier toxicity endpoints.

4.7.2. Reaction mass of 2-ethylhexanoic acid and 2-ethylhexanol and Rhodium tris(2-ethylhexanoate)

Substance	CAS number	Chemical structure
Reaction mass of 2-ethylhexanoic acid and 2-ethylhexanol and Rhodium tris(2-ethylhexanoate)	Not specified	Not specified

The REACH dossier for this substance contains no toxicity data. Within the dossier, the substance has been assigned classifications of Acute Inhalation Toxicity Cat 4, Skin Irritation Cat 2, Eye Irritation Cat 2, Reproductive Toxicity Cat 2, and STOT-SE Cat 3 ("may cause respiratory irritation"). No explanation for these classifications is provided but they appear to be based on the classifications for 2-ethylhexan-1-ol (Acute Inhalation Toxicity Cat 4, Skin Irritation Cat 2, Eye Irritation Cat 2, STOT-SE Cat 3) and 2-ethylhexanoic acid (Reproductive Toxicity Cat 1B).

4.7.3. Dicarbonyl(pentane-2,4-dionato-O,O')rhodium

Substance	CAS number	Chemical structure
Dicarbonyl(pentane-2,4-dionato-O,O')rhodium	14874-82-9	

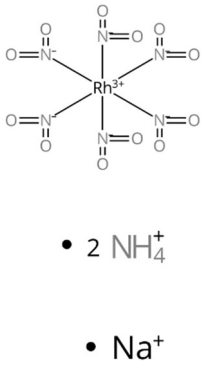
Only a limited toxicity data set under REACH is available for this moderately soluble substance, focusing mainly on in vitro genotoxicity, and acute and local toxicity properties. No repeat-dose toxicity or reproductive toxicity data are available.

Acute oral toxicity data indicate an LD_{50} between 50 and 500 mg/kg body weight, rendering a Cat 3 classification – which is the most stringent acute toxicity classification for the rhodium substances covered in this document. An acute dermal toxicity study, however, found no mortality at 2000 mg/kg body weight and, hence, no classification.

In vivo skin irritation testing showed the substance does not require classification as a skin irritant, while significant irritation was found in an in vivo eye irritation study requiring classification as Eye Irritant Cat 2. It was identified as a skin sensitiser in a Magnussen Kligman test and classified as Skin Sensitiser Cat 1, making it the only Rh(I) compound covered in this document that could be linked to sensitising properties.

Genotoxicity data are limited to an in vitro bacterial mutagenicity test in which there was no evidence of mutagenicity.

4.7.4. Diammonium sodium hexakis(nitrito-N)rhodate

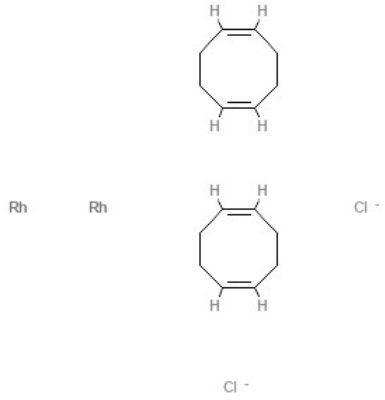
Substance	CAS number	Chemical structure
Diammonium sodium hexakis(nitrito-N)rhodate	64164-17-6	

This substance is characterized as a complex with six ligands of nitrite coordinated to the trivalent metal via the nitrogen atoms. The available short-term toxicity data – which comprise an acute oral toxicity study, skin and eye irritation tests, and a local lymph node assay skin sensitisation test – indicate a low hazard profile not requiring classification.

The battery of in vitro genotoxicity tests performed for this substance did not reveal any empirical concern. However, because this substance is a Rh(III) compound with labile ligands that can be exchanged with chlorine, it cannot be excluded that in the gastric conditions a partial conversion to a (mixed) Rh(III) chloride compound might occur; hence, a precautionary classification as Mutagen Cat 2 is assigned because of the findings with other soluble inorganic Rhodium (III) substances.

No indications of significant systemic toxicity, nor reproductive toxicity were identified in a combined repeated dose and reproductive/developmental toxicity screening study.

4.7.5.D-μ-chloro-bis(hapto-1,5-cyclooctadiene)dirhodium(I)

Substance	CAS number	Chemical structure
D-μ-chloro-bis(hapto-1,5-cyclooctadiene)dirhodium(I)	12092-47-6	

This substance has no toxicity data except for a skin irritation study in which the primary irritation index was 0. The substance has no hazard classifications assigned.

Table 3: Human health hazard classification and toxicity data overview of the Rhodium substances

	CAS number EC number	Acute toxicity			Irritation		Sensitisation		Mutagenicity	Cancer effects	Target organ effects	Repro/ dev effects
		Oral	Dermal	Inhalation	Skin	Eye	Skin	Respiratory				
Elemental rhodium and simple insoluble rhodium substances												
Rhodium	7440-16-6 231-125-0	RA	ND	ND	RA	RA	RA	ND	RA PD	ND	RA PD	ND
Dirhodium trioxide	12036-35-0 234-846-9	D	ND	ND	D	D	D	ND	PD	ND	PD	ND
Rhodium trihydroxide	21656-02-0 244-508-2	RA	ND	ND	RA	RA	RA	ND	D	ND	RA PD	ND
Poorly soluble inorganic Rh (III) substances												
Rhodium triiodide	15492-38-3 239-521-5	ND	ND	ND	ND	ND	ND	ND	PD [b]	ND	ND	ND
Soluble inorganic rhodium (III) substances other than chlororhodate substances												
Rhodium chloride ($RhCl_3$) hydrate / Rhodium trichloride	20765-98-4 606-630-8	D **Cat 4**	D	ND	D **Cat 2**	D **Cat 1**	D **Cat 1**	ND	PD **Cat 2**	ND	D	D
Dirhodium trisulphate	10489-46-0 234-014-5	W	ND	ND	D **Cat 1B**	W **Cat 1**	W [a]	ND	D	ND	ND	ND
Rhodium trinitrate	10139-58-9 233-397-6	D **Cat 4**	ND	ND	D **Cat 1B**	W **Cat 1**	D **Cat 1A**	ND	PD **Cat 2**	ND	D	D
Rhodium acetate	42204-14-8 255-707-9	D	D	ND	D	D **Cat 2**	W	ND	PD & RA **Cat 2**	ND	PD	ND
Complex halogenated rhodium substances												
Triammonium hexachlororhodate	15336-18-2 239-364-2	D	ND	ND	D	D **Cat 1**	ND	ND	PD & RA **Cat 2**	ND	ND	ND
Triphenyl-phosphine Rh substances												
Carbonyl(pentane-2,4-dionato-O,O')(triphenylphosphine)rhodium	25470-96-6 247-015-0	D	ND	ND	D	D	D	ND	PD	ND	PD	ND
Carbonylhydrotris(triphenylphosphine)rhodium	17185-29-4 241-230-3	D	ND	ND	D	D	ND	ND	ND	ND	ND	ND
Tris(triphenylphosphine) rhodium (I) chloride	14694-95-2 238-744-5	D	ND	ND	D	D	D	ND	PD	ND	PD	ND
Other specific rhodium substances												
Dicarbonyl(pentane-2,4-dionato-O,O')rhodium	14874-82-9 238-947-9	D **Cat 3**	D	ND	D	D **Cat 2**	D **Cat 1**	ND	PD	ND	PD	ND
Diammonium sodium hexakis(nitrito-N)rhodate	64164-17-6 264-713-0	D	ND	ND	D	D	D [C]	ND	PD **Cat 2** [d]	ND [c]	D [c]	D [c]
Rhodium tris(2-ethylhexanoate)	20845-92-5 244-079-1	W	ND	ND	D **Cat 1B**	PD **Cat 1**	W	ND	PD	ND	ND	RA **Cat 1B** [e]
Reaction mass of 2-ethylhexanoic acid and 2-ethylhexanol and Rhodium tris(2-ethylhexanoate)	[*not specified*] 947-831-3	ND	ND	**Cat 4** [g]	**Cat 2** [g]	**Cat 2** [g]	ND	ND	ND	ND	**STOT-SE 3**[fg]	**Cat 2** [g]
D-μ-chloro-bis(hapto-1,5-cyclooctadiene)dirhodium(I)	12092-47-6 235-157-6	ND	ND	ND	D	ND	ND	ND	ND	ND	ND	ND

D	**Classification not required**: Data available (D).
RA/PD	**Classification not required**: Partial data available (PD), read-across (RA), partial data and read-across (PD & RA), or read-across of partial data (RA PD).
ND/W	**Classification not required**: No data available (ND) and/or data requirement waived (W).
ND/W	**Classified based on assumed hazard**: No data available (ND) and/or data requirement waived (W).
RA/PD	**Classified**: Partial data available (PD), read-across (RA), partial data and read-across (PD & RA), or read-across of partial data (RA PD).
D	**Classified**: Data available (D).

[a] A skin sensitisation study was waived on the basis the substance is classified as corrosive to skin. In two limited occupational studies, dirhodium trisulphate displayed slight evidence of skin sensitisation potential, insufficient to require classification.

[b] An in vitro bacterial mutagenicity study showed mutagenic activity, but used DMSO as a solvent vehicle, which is inappropriate as it is likely to have complexed with the test material.

[c] Forms of this substance with varying levels of impurities have been classified for additional classifications such as skin sensitisation (Cat 1), reproductive toxicity (Cat 1A), mutagenicity (Cat 2), carcinogenicity (Cat 1A), and STOT-RE 2

[d] based on the existing dataset the substance does not meet currently meet the criteria for classification as a germ cell mutagen Cat 1A or 1B; however, in spite of negative results in vitro genotoxicity testing, the substance was classified as mutagen Cat 2 as a precaution based on anticipated speciation in the in vivo gastric environment (dissociation and binding with chloride ligands).

[e] The substance falls within the scope of the EU harmonized classification for '2-ethylhexanoic acid and its salts' of Repro 1B (H360D).

[f] May cause respiratory irritation.

[g] The REACH dossier for this substance contains no toxicity data. The basis of the classifications for this substance are unclear but appear to be based on those for 2-ethylhexan-1-ol and 2-ethylhexanoic acid.

5. Ruthenium compounds

5.1. Introduction and summary

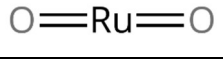
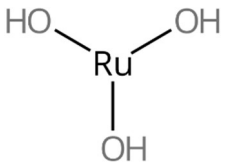
Active EU REACH Registration dossiers for nine ruthenium substances were identified. An overview of the human health hazard classifications and toxicity data for these substances is provided in Table 4. For this purpose, the substances have been grouped as follows. All nine substances in these groups are monoconstituent substances:

- Elemental ruthenium and simple insoluble ruthenium substances
- Soluble ruthenium substances, excluding complex halogenated ruthenium substances
- Complex halogenated ruthenium substances
- Insoluble or poorly soluble complex organic ruthenium substances

Across the groups, toxicity data availability is variable but often limited to studies of acute oral toxicity, skin and eye irritation, skin sensitisation, and limited mutagenicity data, except for the complex halogenated ruthenium substances and other soluble ruthenium substances groups for which more complete mutagenicity data and repeat-dose toxicity and screening level reproductive and developmental toxicity studies are additionally available.

5.2. Elemental ruthenium and simple insoluble ruthenium substances

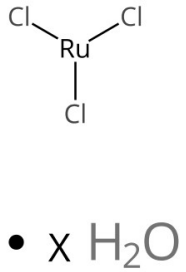
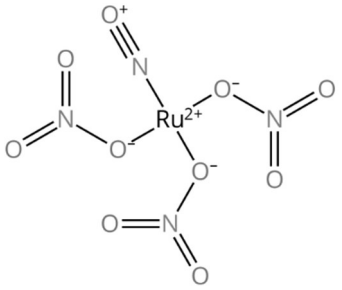
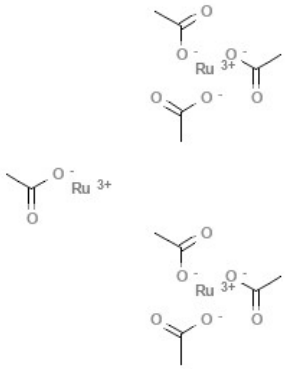
Three substances have been placed in this group: elemental ruthenium, ruthenium (IV) oxide, and ruthenium trihydroxide.

Substance	CAS number	Chemical structure
Ruthenium	7440-18-8	
Ruthenium (IV) oxide	12036-10-1	
Ruthenium trihydroxide	12135-42-1	

No hazard classifications have been assigned to any of these three substances, although there are no toxicity data available for ruthenium trihydroxide. Ruthenium data include acute oral toxicity, in vitro genotoxicity, and a reproductive and general repeat dose toxicity screening study. Ruthenium (IV) oxide has been tested for acute oral toxicity, skin irritation, eye irritation, and skin sensitisation, and also for mutagenic potential in an in vitro bacterial reverse mutation assay. All studies indicated no corresponding hazard classifications were required.

5.3. Soluble ruthenium substances, excluding complex halogenated ruthenium substances

Three substances are in this group: hexakis[μ-(acetato-O:O')]-μ3-oxo-triangulo-triruthenium acetate (colloquially known as ruthenium acetate), tris(nitrato-O)nitrosylruthenium (colloquially known as ruthenium nitrate) and ruthenium trichloride hydrate.

Substance	CAS number	Chemical structure
Ruthenium trichloride hydrate	14898-67-0	
Tris(nitrato-O)nitrosylruthenium	34513-98-9	
Hexakis[μ-(acetato-O:O')]-μ3-oxo-triangulo-triruthenium acetate	55466-76-7	

The latter two substances are acidic and testing has shown them to be corrosive to skin and/or eyes. Skin sensitisation testing was waived based on corrosivity (although not for ruthenium acetate), with no classification for sensitisation assigned. Acute oral toxicity testing of tris(nitrato-O)nitrosylruthenium was also waived due to its corrosivity with no classification for acute toxicity assigned, while an acute oral toxicity study was available for ruthenium trichloride hydrate showing it to require classification as Acute Oral Tox Cat. 4.

The only other data for tris(nitrato-O)nitrosylruthenium are genotoxicity data: in vitro bacterial reverse mutation assay testing in which mutagenic activity was found in *S. typhimurium* strain TA 102 (in both the presence and absence of metabolic activation) and TA98 (-S9), but not in other strains of *S. typhimurium* or *E. coli* WP2 uvrA. It was concluded that this suggests a reactive oxygen species (ROS) mode of action and that consequently the mutagenicity might not carry over to the in vivo

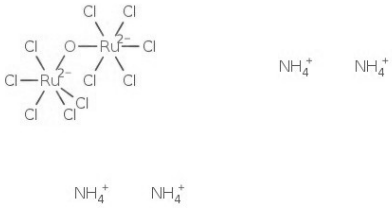
situation. Subsequent in vivo testing has been undertaken which supports this hypothesis and the compound does not require classification for mutagenicity.

Ruthenium trichloride hydrate has a more extensive battery of in vitro genotoxicity tests with bacterial reverse mutation, mouse lymphoma cell gene mutation, and human peripheral blood lymphocyte micronucleus tests, the results of which indicate the substance is not mutagenic. A repeated dose toxicity and reproductive and developmental toxicity screening study is also available for ruthenium trichloride hydrate in which no adverse effects on either general toxicity, reproductive parameters or development of offspring were found, and no classification is assigned.

Hexakis[µ-(acetato-O:O')]-µ3-oxo-triangulo-triruthenium acetate has a slightly different profile and dataset as it is not a skin corrosive and has been tested for acute oral toxicity, acute dermal toxicity, eye irritation, skin sensitisation, in vitro and in vivo genotoxicity, and 28-day repeated dose oral toxicity. The substance was found to be a severe eye irritant requiring classification as Eye Damage Cat 1. Based on the results of all the other studies, no other hazard classifications were required for this substance.

5.4. Complex halogenated ruthenium substances

Only one complex halogenated ruthenium substance is registered under EU REACH: tetraammonium decachloro-µ-oxodiruthenate(4-).

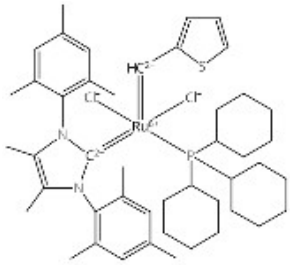
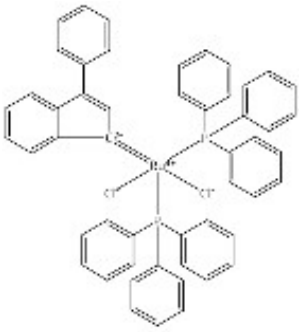
Substance	CAS number	Chemical structure
tetraammonium decachloro-µ-oxodiruthenate(4-)	85392-65-0	

Testing has confirmed this substance to be a severe eye irritant (Eye Damage Cat 1) and a skin sensitiser (Skin Sens Cat 1B). The results of the various other toxicity studies available for this substance, including acute oral toxicity, skin irritation, a suite of in vitro genotoxicity assays, and a combined repeated dose and reproductive and developmental toxicity screening study did not require any other hazard classifications to be assigned.

5.5. Insoluble or poorly soluble complex organic ruthenium substances

Active EU REACH dossiers were found for two insoluble or poorly soluble complex organic ruthenium substances:

- [1,3-bis(2,4,6-trimethylphenyl)-4,5-dimethylimidazol-2-ylidene](2-thienylmethylidene)(tricyclohexylphosphine)ruthenium(II)dichloride]
- Ruthenium, dichloro(3-phenyl-1H-inden-1-ylidene)bis(triphenylphosphine-, (SP-5-31) Coordination compound

Substance	CAS number	Chemical structure
[1,3-bis(2,4,6-trimethylphenyl)-4,5-dimethylimidazol-2-ylidene](2-thienylmethylidene)(tricyclohexylphosphine)ruthenium(II)dichloride]	1190427-50-9	
Ruthenium, dichloro(3-phenyl-1H-inden-1-ylidene)bis(triphenylphosphine-, (SP-5-31) Coordination compound	254972-46-8	

Both substances have been tested for acute oral toxicity, skin irritation, eye irritation, skin sensitisation, and in vitro genotoxicity (bacterial reverse mutation test only). Based on the results of these studies, [1,3-bis(2,4,6-trimethylphenyl)-4,5-dimethylimidazol-2-ylidene](2-thienylmethylidene)(tricyclohexylphosphine)ruthenium(II)dichloride] was concluded to be a skin sensitiser (Cat 1) but no other hazard classifications were required. No hazard classifications were required for Ruthenium, dichloro(3-phenyl-1H-inden-1-ylidene)bis(triphenylphosphine-, (SP-5-31) Coordination compound.

For determining skin sensitisation potential, each of the two substances was tested in a Local Lymph Node Assay (LLNA). Ruthenium, dichloro(3-phenyl-1H-inden-1-ylidene)bis(triphenylphosphine-, (SP-5-31) Coordination compound was tested at concentrations of 10%, 25% and 50% which produced Stimulation Indices (SI) of 1.5, 2.3 and 2.4, respectively, i.e. below the threshold of 3. It is noted in the dossier that the test material concentration, if any, that will give an SI of 3 or more exceeds 50%. In the LLNA study of [1,3-bis(2,4,6-trimethylphenyl)-4,5-dimethylimidazol-2-ylidene](2-thienylmethylidene)(tricyclohexylphosphine)ruthenium(II)dichloride], test concentrations of 6.25%, 12.5% and 25% were used, producing SI values of 4.7, 4.2 and 3.2, respectively – i.e. an inverse dose-response.

Table 4: Human health hazard classification and toxicity data overview of the ruthenium substances

	CAS number EC number	Acute toxicity			Irritation		Sensitisation		Mutagenicity	Cancer effects	Target organ effects	Repro/ dev effects
		Oral	Dermal	Inhalation	Skin	Eye	Skin	Respiratory				
Elemental ruthenium and simple insoluble ruthenium substances												
Ruthenium	7440-18-8 231-127-1	D	W	W	W	W	W	ND	D	ND	PD	W
Ruthenium (IV) oxide	12036-10-1 234-840-6	D	ND	ND	D	D	D	ND	PD	ND	PD	ND
Ruthenium trihydroxide	12135-42-1 235-221-3	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Soluble ruthenium substances, excluding complex halogenated ruthenium substances												
Ruthenium trichloride hydrate	14898-67-0 604-667-4	D **Cat 4**	ND	ND	D **Cat 1B**	W **Cat 1**	W	ND	D	ND	D	D
Tris(nitrato-O)nitrosylruthenium	34513-98-9 252-068-8	W	ND	ND	D **Cat 1B**	W **Cat 1**	W	ND	D[a]	ND	ND	ND
Hexakis[μ-(acetato-O:O')]-μ3-oxo-triangulo-triruthenium acetate	55466-76-7 259-653-7	D	D	ND	D	D **Cat 1**	D	ND	D	ND	D	ND
Complex halogenated ruthenium substances												
Tetraammonium decachloro-μ-oxodiruthenate(4-)	85392-65-0 286-924-7	D	ND	ND	D	D **Cat 1**	D **Cat 1B**	ND	D	ND	D	PD
Insoluble or poorly soluble complex organic ruthenium substances												
[1,3-bis(2,4,6-trimethylphenyl)-4,5-dimethylimidazol-2-ylidene](2-thienylmethylidene)(tricyclohexylphosphine)ruthenium(II)dichloride]	1190427-50-9 682-131-9	D	ND	ND	D	D	D **Cat 1**	ND	PD	ND	PD	ND
Ruthenium, dichloro(3-phenyl-1H-inden-1-ylidene)bis(triphenylphosphine-, (SP-5-31) Coordination compound	254972-46-8 664-479-3	D	ND	ND	D	D	D	ND	PD	ND	PD	ND

D **Classification not required**: Data available (D).

RA/PD **Classification not required**: Partial data available (PD), read-across (RA), partial data and read-across (PD & RA), or read-across of partial data (RA PD).

ND/W **Classification not required**: No data available (ND) and/or data requirement waived (W).

ND/W **Classified based on assumed hazard**: No data available (ND) and/or data requirement waived (W).

RA/PD **Classified**: Partial data available (PD), read-across (RA), partial data and read-across (PD & RA), or read-across of partial data (RA PD).

D **Classified**: Data available (D).

[a] testing inconclusive. Substance not classified but further testing proposed.

6. Iridium compounds

6.1. Introduction and summary

Active EU REACH Registration dossiers for three iridium substances were identified: elemental iridium, and two chloroiridate substances – hexachloroiridic acid (UVCB) and diammonium hexachloroiridate.

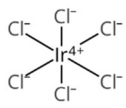
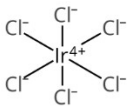
An overview of the human health hazard classifications and toxicity data for these iridium substances is provided in Table 5.

6.2. Elemental iridium

Substance	CAS number	Chemical structure
Iridium	7439-88-5	Ir

Elemental iridium has not been assigned any human health hazard classifications. It has been tested for acute oral toxicity, skin and eye irritation, skin sensitisation, and in vitro bacterial mutagenicity.

6.3. Complex halogenated iridium substances

Substance	CAS number	Chemical structure
Hexachloroiridic acid	16941-92-7	 • 2 H^+
Diammonium hexachloroiridate	16940-92-4	 • 2 NH_4^+

Note: the structures depicted for UVCB substances are for illustration only and do not necessarily represent the real-world ratios of the constituents, nor the dynamic intra and inter-molecular structural interactions.

Diammonium hexachloroiridate is registered as a monoconstituent substance, while hexachloroiridic acid (also known as dihydrogen hexachloroiridate) is registered as a UVCB. Acute oral toxicity data are available for both substances, requiring classification as Acute Toxicity Cat 4. No dermal or inhalation acute toxicity data are available.

6.3.1. Diammonium hexachloroiridate

Diammonium hexachloroiridate was found to be non-irritating to skin in an in vitro skin irritation test (reconstructed human epidermis test), while the results of two different in vitro eye irritation tests (Bovine Corneal Opacity and Permeability Test and reconstructed human cornea-like epithelium test) indicated it requires classification but the test results did not allow discrimination as to whether it should be classified as Cat 1 or Cat 2. It was assigned an Eye Damage Cat 1 classification to avoid further (in vivo) testing. Diammonium hexachloroiridate was concluded to not possess skin sensitisation potential when tested in a Local Lymph Node Assay (LLNA). Genotoxicity data for diammonium hexachloroiridate are limited to an in vitro bacterial reverse mutation study using five strains of *S. typhimurium* in which the test substance was concluded to be non-mutagenic both with and without metabolic activation.

6.3.2. Hexachloroiridic acid

Based on the results of an in vivo test, hexachloroiridic acid was concluded to be corrosive to skin and assigned a classification of Skin Corrosion Cat 1C. Consequently, eye irritation testing was waived and the substance was automatically classified as Eye Damage Cat 1. Skin sensitisation testing was similarly waived based on the acidic and corrosive nature of the substance. The substance was not classified for skin sensitisation. It was noted there is a published report of a worker with occupational respiratory and skin symptoms showing a positive reaction on prick and skin testing with hexachloroiridic acid while showing no evidence of platinum sensitisation, but this isolated case report is an insufficient basis upon which to classify the substance.

Genotoxicity data for hexachloroiridic acid comprise two limited in vitro bacterial assays: a *Bacillus subtilis* recombination assay in which the authors concluded the results were indicative of a mild positive effect, and a spot test reverse mutation assay using five strains of *S. typhimurium* and two strains of *E. coli* without metabolic activation in which the test substance did not cause mutations. Based on these data, the substance does not require classification for mutagenicity; though both studies had limitations and do not permit a confident conclusion on mutagenic potential.

Table 5: Human health hazard classification and toxicity data overview of the Iridium substances

	CAS number EC number	Acute toxicity			Irritation		Sensitisation		Mutagenicity	Cancer effects	Target organ effects	Repro/ dev effects
		Oral	Dermal	Inhalation	Skin	Eye	Skin	Respiratory				
Elemental Ir and simple insoluble Ir substances												
Iridium	7439-88-5 231-095-9	D	ND	ND	D	D	D	ND	PD	ND	PD	ND
Complex halogenated iridium substances												
Hexachloroiridic acid	16941-92-7 241-012-8	D **Cat 4**	ND	ND	D **Cat 1C**	W **Cat 1**	W [b]	ND	PD [a]	ND	ND	ND
Diammonium hexachloroiridate	16940-92-4 241-007-0	D **Cat 4**	ND	ND	D	PD [c] **Cat 1**	D [d]	ND	PD	ND	PD	ND

D **Classification not required**: Data available (D).

RA/PD **Classification not required**: Partial data available (PD), read-across (RA), partial data and read-across (PD & RA), or read-across of partial data (RA PD).

ND/W **Classification not required**: No data available (ND) and/or data requirement waived (W).

ND/W **Classified based on assumed hazard**: No data available (ND) and/or data requirement waived (W).

RA/PD **Classified**: Partial data available (PD), read-across (RA), partial data and read-across (PD & RA), or read-across of partial data (RA PD).

D **Classified**: Data available (D).

[a] Only two bacterial studies are available: one showed indications of possible DNA damage while the other showed no evidence of mutations.

[b] Skin sensitisation study was waived as the substance is acidic and classified for skin corrosion. There is a published report of a worker with occupational respiratory and skin symptoms showing a positive reaction on prick and skin testing with hexachloroiridic acid while showing no evidence of platinum sensitisation.

[c] The results of the two in vitro eye irritation studies available collectively do not enable discrimination between whether the substance should be classified as Cat 1 or Cat 2. The substance was classified by the manufacturer as Cat 1 to avoid further (animal) testing.

[d] Toxicology sensitisation testing was negative. In human patch testing of 210 dental alloy patients, one person showed a weak reaction.