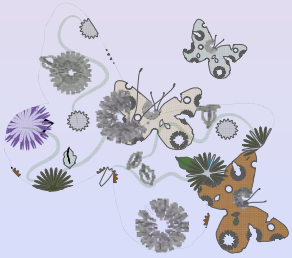
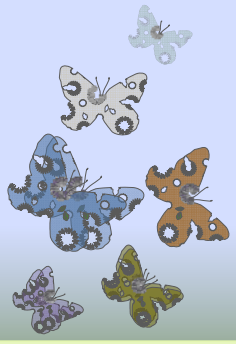
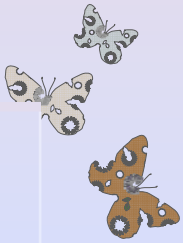
Rhenium Project Progress



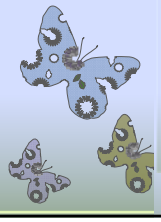


WCA Environment Ltd & bibra

Presentation outline



- Overall Project Progress
- Phys-chem and environmental sections
- Mammalian toxicology section
- REACH requirements
- Testing strategies
- Laboratories
- CSA/CSR
- IUCLID 5
- Exposure
- Timelines
- Budget
- Key decisions



Current status

- Phase I = complete
- Phase II = in progress and ahead of the schedule in the proposal
- Phase III = in progress and ahead of the schedule in the proposal

Overall Project Progress

Phase II:

- Identification and review of all relevant studies, and preparation of robust summaries and Klimisch scores for each critical study;
- Construction of a matrix with the available information for each category;
- Evaluation of the physicochemical parameters for each category and assess category viability;
- Evaluation of the mammalian and ecotoxicity data for category justification;
- Evaluation of the relevant information for individual substance registration;
- Identification of potential read-across;
- Identification of test waivers;
- Application of REACH derogations (in particular related to Annex III);
- Recommendation of testing strategies; and
- Production of a draft report.

Phase III:

- Test Programme Design
- Study monitoring

Progress: Phys-chem and Environmental Sections

PHASE II: TEST DEROGATION ASSESSMENT	
Acquire publications and proprietary reports	✓
Assign Klimisch scores	✓
Apply Annex XI / read across / waivers if gaps	✓
Check viability of categories	In progress
Identify real data gaps	✓
Assign value to proprietary data	?
Develop test plan (incl. adaptations and new testing)	In progress
Check PBT/vPvB	NA
PHASE III: TEST PROGRAMME DESIGN	
	In progress

Mammalian Toxicology

Only very limited data were identified in Phase I searches, or made available by PMC members.

- An attempt to identify additional data that may usefully contribute using the **bibra** TRACE database failed to find relevant data on other rhenium compounds.
- In fact, only **two** (early) studies were available, both for ammonium perrhenate.
- These have been scored to indicate acceptable reliability. Robust study summaries have been prepared using IUCLID 5 templates:

Ammonium perrhenate (CAS 13598-65-7)

REACH Endpoints

8.1 **Skin irritation**

- Available data indicate not irritating to rabbit skin.

8.5.1 **Acute toxicity, oral route**

- Available data indicate rat LD50 > 2 g/kg bw.

Mamm tox: possibilities for read-across / data-waiving

- Although only limited data exist, these can be used, together with rules for adaptation (Column 2 - annexes VII & VIII) from standard information requirements (Column 1 - annexes VII & VIII), and data generated for ammonium perrhenate, to minimize the need for testing:

- Perrhenic acid - corrosive?
- Dirhenium heptaoxide - corrosive?

Mamm tox cont. Ammonium perrhenate - data gaps that need to be filled:

1) *in vitro* eye irritation - if negative, then *in vivo*

2) skin sensitization

3) *in vitro* gene mutation study in bacteria(?)

4) *in vitro* cytogenicity in mammalian cells

5) *in vitro* gene mutation study in mammalian cells

(*in vivo* genotoxicity testing if any positive *in vitro* data)

6) acute toxicity (one other route - dermal?)

7) short term repeated dose toxicity (28 days) [unless relevant human exposure can be excluded]

8) reproductive toxicity (screening for reproductive / developmental toxicity) [unless relevant human exposure can be excluded]

(7) & (8) can be combined using OECD 422

- **Data generated for ammonium perrhenate could potentially be used to fill remaining data gaps(?)**

REACH Requirements

Category	Substance name	CAS number	Type	Tonnage	REACH REQUIREMENT
Re 0	Rhenium	7440-15-5	Substance	1-10	Annex VII
Re 7	Perrhenic acid	13768-11-1	Substance	1-10	Annex VII
	Dirhenium heptaoxide	1314-68-7	Substance	1-10	Annex VII
	Sodium rhenate	13472-33-8	Intermediate	1-10	data that are already available
	Dirhenium heptasulphide	12038-67-4	Intermediate	1-10	data that are already available
Re 7a	Ammonium perrhenate	13598-65-7	Substance	10-100	Annexes VII- VIII

Indicative List, dated 9th September 2009

- **Physicochemical Endpoints**

Annex VII: State of the substance at 20°C and 101.3 kPa; Melting/freezing point; Boiling point; Relative density; Vapour pressure; Surface tension; Water solubility; Partition coefficient n-octanol/water; Flash-point; Flammability; Explosive properties; Self-ignition temperature; Oxidising properties; Granulometry (particle size distribution).

Annex VIII: No further requirements

- **Mammalian Toxicology Endpoints**

Annex VII: Skin irritation *in vitro;* Eye irritation *in vitro;* Skin sensitisation *In vitro;* gene mutation study in bacteria; Acute toxicity, oral route.

Annex VIII: Skin irritation *in vivo;* Eye irritation *in vivo;* *In vitro* cytogenicity in mammalian cells; *In vitro* gene mutation study in mammalian cells; Acute toxicity, inhalation; Acute toxicity, dermal route; Short-term repeated dose toxicity oral/dermal/inhalation; Reproduction toxicity; Developmental toxicity; Assessment of toxicokinetic behaviour (based on required studies).

- **Ecotoxicology Endpoints**

Annex VII: Short-term toxicity testing on aquatic inverts (preferably *Daphnia*); Growth inhibition study on aquatic plants (preferably algae) .

Annex VIII: Short-term toxicity testing on fish

- **Environmental Fate Endpoints**

Annex VII: Biodegradation in water: screening tests

Annex VIII: Activated sludge respiration inhibition testing; Hydrolysis as a function of pH and identification of degradation products; Adsorption/desorption screening study (HPLC method).

Phase III: Testing Strategies

- UV Spectroscopy (OECD 101) and ICP-OES analysis (proposal by Dr Mitchell) for all substances and intermediates (6 in total)

- ISSUES
  - Contact made with the Fraunhofer Institut – no capacity for any testing until at least January 2010.
  - Other labs contacted and quotes received – Wildlife International, Aqura, Intertek
  - Further testing would be required to fulfil REACH requirements
  - Obtaining samples from Sigma - issue with sameness (to be discussed later)

WCA Testing Strategy – Phys-chem

Test required	CAS Number	Number of tests	Comment	Cost from Aqura	Cost from Intertek
Melting/freezing point	13768-11-1	2		€1560 per test	awaiting quote
	12038-67-4				
Boiling point	13768-11-1	2	Dependent on outcome of mpt testing	€1560 per test	awaiting quote
	12038-67-4				
Water solubility	7440-15-5	4	T/D testing	€ 10,870	awaiting quote
	13768-11-1		OECD 105	€2500 per test	approx. €2000 per test
	1314-68-7				
	12038-67-4				
Flammability	7440-15-5	5		€1700 per test	awaiting quote
	13768-11-1				
	1314-68-7				
	12038-67-4				
	13598-65-7				
Self-ignition temperature	13768-11-1	4	Dependent on outcome of mpt testing	€1700 per test	awaiting quote
	1314-68-7				
	12038-67-4		Dependent on outcome of mpt testing		
	13598-65-7				
Oxidising properties	13768-11-1	2		€4900 per test	awaiting quote
	1314-68-7				
Granulometry (particle size distribution)	1314-68-7	3		€990 per test	awaiting quote
	12038-67-4				
UV - VIS Spectroscopy				€620 per test	approx. €500 per test

Transformation and Dissolution testing

- For sparingly soluble substances (indicative solubility <µg/l)
- provide an indication of the solubility of the metal and of any transformation of the metal to an environmentally stable ion or substance.
- carried out at three different pHs
- information throughout 28 days
- UV-VIS test can be co-ordinated with this test and will provide information on the long-term stability

Category	Re 0	Re 7				Re 7a
CAS number	7440-15-5	13768-11-1	1314-68-7	13472-33-8	12038-67-4	13598-65-7
State of the substance at 20°C and 101.3 kPa						
Melting/freezing point						
Boiling point						
Relative density						
Vapour pressure						
Surface tension						
Water solubility						
Partition coefficient n-octanol/water, flask shake method						
Flash-point						
Flammability						
Explosive properties						
Self-ignition temperature						
Oxidising properties						
Granulometry (particle size distribution)						

Key	
	Testing required
	Testing requirement dependent on outcome of other tests or read-across to data not yet available because the test on the read-across substance has not been commissioned or performed
	Data available, adaptation available, read-across to available data
	Intermediate - data not a requirement

WCA Testing Strategy – Ecotox and Environmental Fate

Test required	CAS Number	Number of tests	Comment	Cost from Aqura	Cost from Intertek
Short-term toxicity testing on aquatic invertebrates (preferably *Daphnia*)	1314-68-7	2		€2100 per test (accompanying analytics (ICP-OES) = €2000-3500)	awaiting quote
	13598-65-7				
Growth inhibition study on aquatic plants (preferably algae)	1314-68-7	2		€2480 per test (accompanying analytics (ICP-OES) = €2000-3500)	
	13598-65-7				
Short-term toxicity testing on fish	13598-65-7	1		€2420 per test (accompanying analytics (ICP-OES) = €2000-3500)	

Test required	CAS Number	Cost from Aqura	Cost from Intertek
Activated sludge respiration inhibition testing	13598-65-7	€ 1,870	awaiting quote

Category	Re 0	Re 7				Re 7a
CAS number	7440-15-5	13768-11-1	1314-68-7	13472-33-8	12038-67-4	13598-65-7
Short-term toxicity testing on aquatic inverts (preferably *Daphnia*)						
Growth inhibition study on aquatic plants (preferably algae)						
Short-term toxicity testing on fish						

Category	Re 0	Re 7				Re 7a
CAS number	7440-15-5	13768-11-1	1314-68-7	13472-33-8	12038-67-4	13598-65-7
Biodegradation in water: screening tests						
Activated sludge respiration inhibition testing						
Hydrolysis as a function of pH and identification of degradation products						
Adsorption/desorption screening study (HPLC method)						

Key	
	Testing required
	Testing requirement dependent on outcome of other tests or read-across to data not yet available because testing on the reas-across substance has not been commissioned or performed
	Data available, adaptation available, read-across to available data
	Intermediate - data not a requirement

Laboratories

- **Aqura**
  - Quote for all required tests has been received, including costs and sample quantities.
  - could start with the studies (at first: paperwork, GLP protocols) within 2 weeks, followed with the laboratory work (except water solubility which they could start at the beginning of November). The necessary time for the studies depends on the parameters: 4 weeks to 3 months.
- **Intertek**
  - We are awaiting a quote covering all the test requirements. We have previously received quotes for water solubility testing (OECD 105) and UV spectroscopy (OECD 101).

T/D testing labs

- Several laboratories have been contacted about T/D testing specifically.

1. ITRI
2. CANMET
3. Aqura

Varying costs, capacity and experience

Phase IV: CSA/CSR

1. IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES – Individual companies and WCA
2. MANUFACTURE AND USES – Individual companies and WCA
3. CLASSIFICATION AND LABELLING - WCA and bibra
4. ENVIRONMENTAL FATE PROPERTIES - WCA
5. HUMAN HEALTH HAZARD ASSESSMENT - bibra
6. HUMAN HEALTH HAZARD ASSESSMENT OF PHYSICO-CHEMICAL PROPERTIES – WCA and bibra
7. ENVIRONMENTAL HAZARD ASSESSMENT - WCA
8. PBT AND VPVB ASSESSMENT – WCA and bibra
9. EXPOSURE ASSESSMENT - WCA
10. RISK CHARACTERISATION - WCA

Phase IV: CSA/CSR cont.

- Not as straightforward as pressing a button!
- Certain sections of IUC5 do not get transferred automatically into the CSR format
- WCA have generated templates for these sections which are inserted
- Formatting issues
- Internal and external reviews and subsequent changes

Phase IV: CSA/CSR cont.

- **Individual company inputs**
  - See Handout with fields from Chapter 1
  - Exposure data
- **Category Justification Documents**
  - Information on impurities and composition required from each company
  - Sameness issue

Phase V: IUCLID 5

- **Bibliographic input**
  - Before full bibliographic details can be entered onto IUC5 letters of access required
- **IUCLID Hosting?**
  - Email IUC files around – not very secure, more potential for errors
  - Dedicated server or virtual server

Exposure

- Questionnaire
  - Word format
  - Refined version of the multimetallic questionnaire
  - Mechanism of distribution
  - Deadlines/Timelines
- None classified
  - We will need to evaluate mamm tox and ecotox data before exposure data requirement known.

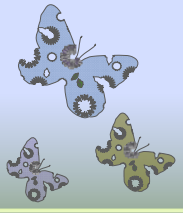
Timelines

- **Deadlines in proposal**

Phase II: Completion within 12 months after Phase I completion - 28.11.2008-27.11.2009. The go ahead for the Phase II pilot was given in December 2008. The formal approval for the full phase II was given in July 2009. However we started work informally in May 2009.

- **Meeting 2010 registration deadline**
  - Dependent on many factors: agreement of testing strategy, which laboratory to use, laboratory capacity, review of reports, receipt of exposure data etc.

Budget



Key decisions

- IUCLID 5
- Testing recommendations
- Testing Labs
- Exposure