PRECIOUS METALS & RHENIUM CONSORTIUM

TENDER FOR PLATINUM GROUP METALS AND RHENIUM REACH REGISTRATION PROJECTS

PROPOSAL FROM WCA ENVIRONMENT & BIBRA

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Introduction

The Precious Metals Consortium (PMC) has invited WCA Environment and bibra to tender for Platinum Group Metals (PGMs) and Rhenium REACH Registration projects. The three projects are based on five phases of work, as follows:

- Phase I: Literature work; data gap analysis; formal report of findings.
- Phase II: Test derogation assessments and the design and progression of any enabling tests (such as bioaccessibility determinations) relevant to Intelligent Testing Strategies and test waiving.
- Phase III: Main test programme design, test conduct, test monitoring and reporting (per REACH Annexes).
- Phase IV: Production of Chemical Safety Assessments/Chemical Safety Reports.
- Phase V: Compilation of IUCLID 5 files and Registration Dossiers.

The numbers of substances for each project are:

- PGMs – 68 substances
- Rhenium – 7 substances

All the listed substances fall within 1-10 or 10-100 tonnes per year bands, and some are intermediates.

The following sections detail the type of work required for each of the five phases, described separately, where necessary, for human health and environmental components, and provide our financial offer. We also provide pen portraits for team members and describe how WCA and bibra staff will work together as a team under the leadership of Dr Mark Crane and within WCA's certified Quality System.

It has been recognised by the PMC that accurate costing of currently unknown quantities of work is not possible. In this proposal we therefore provide a fixed price quote for the elements in Phase I that can be estimated reasonably accurately. We then provide indicative prices for subsequent phases. This revision has been produced after discussion between the PMC TAP and WCA Environment in Brussels on 4th June 2008. Categories/groupings coupled to dossier cloning techniques will be utilised wherever feasible to limit the number of unique dossiers needed (e.g. as might be applicable to closely related substances in a category, and isolated intermediates)

Methodology

PHASE I: LITERATURE REVIEW AND DATA GAP ANALYSIS

The output of Phase I will be a data matrix which clearly identifies tonnage-relevant IUCLID 5 endpoints for which there are no data, tonnage-relevant endpoints for which valid data potentially exist for PGMs and rhenium, and any other toxicity data on these compounds that could be useful in later phases (e.g., when writing data waivers). This will help to provide a preliminary identification of data gaps and endpoints for which grouping and read-across may be possible, and will also help us to identify any appropriate reference substances on the basis of chemical, physical and biological behaviour in relation to other group members (i.e., any trends across groups). We will use experience gained through the understanding of previous metals risk assessments, undertaken through the TCNES process, to assess potential read-across conditions. We will also perform a REACH Annex III

assessment to identify substances for which it is predicted that establishing only a physico-chemical dataset will be required.

We will request and collate all relevant information currently held by members of the PMC, and the following databases will also be searched for information on physical and chemical parameters and toxicological information for mammalian and environmental receptors:

- ChemFinder.com
- Hazardous Substance Databank (HSDB)
- European Inventory of Existing Commercial Chemical Substances (EINECS)
- Toxicological Data Network (TOXNET)
- Ecotox Database (www.epa.gov.ecotox)
- European Chemicals Bureau (ECB) (www.ecb.jrc.it)
- Organisation for Economic Co-operation and Development (OECD) (www.oecd.org)
- Syracuse Research Corporation (www.syrres.com)
- Japan Existing Chemicals Database (JECDB) (http://dra4.nihs.go.jp/mhlw_data/jsp/SearchPageENG.jsp)
- Bibra's TRACE database
- Web of Science
- Google

We have performed an initial search on Toxline and the USEPA Ecotox databases to quantify the approximate number of papers and reports that would need to be screened for each substance. For reasons of member company confidentiality we cannot provide a full breakdown of this analysis here by substance, but we are able to provide an overall summary of the scale of the task.

Toxline shows that there are very large numbers of papers potentially related to mammalian toxicity for PGMs and rhenium as follows:

- Rhenium – 160

Most of these papers are likely not to be of use in fulfilling REACH data requirements, but it is important at least to scan the titles or abstracts to ensure that those that may be of use are identified for further evaluation in the next project Phase. The REACH Regulation puts much emphasis on the obligations on registrants to collect all available and appropriate data. To scope this Phase accurately we sampled the Toxline database to estimate the proportion of papers that could immediately be discarded on the basis of their titles, and the proportion which would require further evaluation of abstracts before a decision could be made. We found the following:

- Rhenium: 50% of papers can be discarded on the basis of their title and 50% require assessment of abstracts.

Assessing *and recording* the results of each assessment takes on average one minute when a title is the basis for a decision and five minutes when an abstract is the basis for a decision. This leads to the following time estimates for the task:

- Rhenium: 8 hours (~ 1 staff day)

A second option would be to select papers from those in the databases which may be of relevance and *not* to document the ones which were discarded on the basis of title alone. This is normal custom and professional practice in other work that we perform for regulatory clients. If this option was selected the time required to perform the screening exercise would be reduced and hence this phase would have a lower cost. This second option would require the following inputs of staff time:

- Rhenium: 8 hours (~ 1 staff day)

A third option, specifically for the PGMs, would be to include use of authoritative published reviews, such as those by the WHO for platinum and palladium, as a baseline and to conduct additional searches only for the years subsequent to the search date in the published review. This is also normal custom and professional practice in other work that we perform for regulatory clients and it has the advantage of focusing the literature search where it is most needed. On this basis the following staff inputs would be required:

- Rhenium: 8 hours (~ 1 staff day)

A search of the Ecotox database shows that there are rather few data (PGMs = 11 and rhenium = 1) so all ecotoxicity data will be included for further analysis in Phase II. Collation of the physicochemical properties and the ecotoxicity data will require an additional 120 hours of staff input.

For substances falling into the 1 – 10 tonnes per year band data should normally be provided during Registration for the following environmental endpoints, as stipulated in REACH Annex VII:

- Physicochemical properties
    - State at 20°C and 103.3 kPa
    - Melting/freezing point
    - Boiling point
    - Relative density
    - Vapour pressure
    - Surface tension
    - Water solubility
    - Partition coefficient
    - Flash point
    - Flammability
    - Explosive properties
    - Self-ignition temperature
    - Oxidising properties
    - Granulometry

Note that not all of the properties listed above are required for all substances. For example, the partition coefficient and flash point are not required for any inorganic substance:

- Toxicological properties
    - Skin irritation or corrosion (based on available data, acid/alkaline reserve or *in vitro* data)

    - Eye irritation (based on available data, acid/alkaline reserve or *in vitro* data)
    - Skin sensitisation (based on available or *in vivo* LLNA data)
    - *In vitro* gene mutation
    - Oral acute toxicity

- Ecotoxicological properties
    - Short-term toxicity to aquatic invertebrates (preferably *Daphnia*)
    - Growth inhibition of aquatic plants (preferable algae)

Note that ready biodegradability studies are not required for inorganic substances.

For substances in the tonnage band of 10-100 tonnes per year the following minimum information is required, in addition to the parameters listed above, as stipulated in REACH Annex VIII:

- Physicochemical properties
    - Hydrolysis as a function of pH
    - Adsorption/desorption screening

- Toxicological properties
    - *In vivo* skin irritation
    - *In vivo* eye irritation
    - *In vitro* cytogenicity
    - Acute inhalation toxicity
    - Acute dermal toxicity
    - Short-term repeated dose toxicity
    - Reproductive/developmental toxicity screen
    - Toxicokinetics (if data are available)

Note that there are many opportunities for presenting technical arguments for waiving many of these tests on the basis of likely exposure or toxicity.

- Ecotoxicological properties
    - Short-term toxicity to fish
    - Activated sludge respiration inhibition

Note that degradation studies are not required for inorganic substances.

For on-site isolated intermediates used under strictly controlled conditions, the information requirements on substance intrinsic properties (physicochemical, human health and environment properties) are reduced to existing readily available data (according to Articles 17 and 18) held by the manufacturer, or "obtainable from other sources". WCA currently interprets this within the context of a consortium such as the PMC as meaning that this rather vague requirement will be met sufficiently for the purposes of the ECHA if all members of the PMC agree to share their data on isolated intermediates. Therefore, the time required to search for these substances could be substantially reduced. However, if read-across is to be effective then it is important that all relevant data are used, so we do not recommend constraining the search for data for isolated intermediates in this Phase.

Once potentially useful data have been identified we will produce separate matrices for PGM (six in total) and rhenium. These matrices will identify the total number of potential studies available for each tonnage-relevant endpoint, although the quality of these studies and therefore their suitability for fulfilling REACH requirements will not be known until work is undertaken in the next phase. The

matrices will clearly identify required IUCLID endpoints for which there are no data (and for which read across, exposure-based waiving, or testing may be required). The matrices will allow us to scope and price the next Phase of work more accurately because we will know the precise number of studies that need to be reviewed. The matrices would be accompanied by a succinct report describing the search strategy and findings, and spreadsheets detailing the decisions made about each of the study titles (option 1) or abstracts (options 2 and 3) reviewed in this Phase.

This Phase of the project would be performed exclusively by, and be the sole responsibility of, WCA Environment limited (Mark Crane, Graham Merrington, Adam Peters and Albania Grosso). The PMC TAP agreed on 6th June 2008 that Option 1 for rhenium and option 3 for PGMs is their preferred option, and that the initial start-up meeting held on June 6th should be followed by one more face to face meeting during this Phase (most likely in September 2008). The total charge for these options and for meeting attendance is £31250. We are able to offer a fixed price for this Phase because unknown variables, such as the number of papers that would subsequently require detailed analysis, are considered only in later Phases. This task would be completed within four months of project inception.

PHASE II: TEST DEROGATION ASSESSMENT

The output of Phase II will be a set of fully quality assured data for each substance or category, final identification of data gaps, and carefully argued cases for any test waivers on the basis of their likely importance in either an environmental or human health risk assessment.

Potentially relevant data identified in Phase I will be scored for quality (Klimisch score of 1 – 4). Studies scored 1 or 2 will be carried forward in the assessment. Studies with a score of 3 (invalid) will not be used further, and the reasons for this will be documented. Studies receiving a score of 4 (non-assignable) will only be used to support the results from studies scored 1 or 2, if this is necessary. Ten per cent of the data, selected at random, will be reassessed by another member of staff as part of our Quality Assurance system. Both HERAG (Fact Sheet 6) and MERAG (Fact Sheet 3) will be considered during this phase of the project. When necessary we will at this stage also extend the search for relevant data beyond those substances that the PMC wishes to Register. For example, there may be substances (e.g., osmium) for which very little data is available for the substances that are to be registered and it may be useful to extend the search to other compounds with the same metal to read across and to use in a weight of evidence approach for the assessment.

Once the data gap analysis is complete, a detailed assessment of the potential for test derogation and read-across from one substance to another can be conducted. The main basis for test derogation will be the potential for scientifically-based grouping of substances in the PGMs and rhenium categories. The European Commission's Joint Research Centre and OECD have provided guidance and examples of when this is likely to be defensible[1,2]. For metals, the general approach taken for cadmium, copper and nickel during risk assessments has been to consider the available data, including differences in the chemistry that are likely to lead to different physical or biological behaviour, particularly (bio)availability (cf. MERAG), and then to read across from a realistic worst-case value to ensure conservatism. When sufficiently reliable data are not available for read-across there is consideration of whether the absence of such data might be critical for risk characterisation, given likely exposure

[1] Worth A Patlewicz G. 2007. A compendium of case studies that helped to shape the REACH guidance on chemical categories and read across. EC JRC EUR 22481, Ispra, Italy.
[2] OECD. Guidance on grouping of chemicals. 2007. Organisation for Economic Co-operation and Development Environment Health and Safety Publications. Series on Testing and Assessment No. 80, Paris, France.

scenarios. If evidence suggests that exposure of particular receptors (e.g., aquatic environment, human occupational exposure) is unlikely to occur, a case can be made for test derogation.

This general approach has been accepted by the Commission during risk assessments of metals and is therefore the approach that we would use when considering whether testing is necessary to fill data gaps. We would follow these steps to achieve a defensible grouping:

1. Analyse available physicochemical data on each substance to determine whether there are any fundamental differences, particularly in metal ion oxidation state, water solubility, crystalline structure or particle size.

2. Compare differences in solubility, bioaccessibility and other physicochemical data with available data on toxicity to humans or the environment, and to any available toxicokinetic data.

3. Examine the possible influence of any counter ions.

If by following these steps there is still insufficient information to place a substance in a category, OECD[2] (with substantial input from EC JRC) recommends that *in vitro* approaches, such as examination of relative solubilities in physiological media, might be a way of avoiding the need for *in vivo* data.

This Phase of the project would be performed by staff at WCA Environment limited (Mark Crane, Graham Merrington, Adam Peters, Chris Watts and Albania Grosso) and bibra (where James Hopkins, Pete Watts, Philip Copestake and Tanya Diver will be responsible for the quality of the evaluations), with the former assessing physicochemical and ecotoxicological data, and the latter assessing mammalian toxicology data. It is not possible at this stage to identify the overall charge for this Phase because this depends on the number of studies that emerge from Phase I which need to be assessed. An indicative price is £10000 (ten thousand pounds sterling; excl. VAT) per substance/category, with the minimum possible number of categories equalling eight. This estimate is based on an average of one study per tonnage-relevant endpoint per substance/group (i.e., there may be several studies for some endpoints and none for others – we have averaged these across all studies required per tonnage band to arrive at an indicative charge). However, substances are likely to need to be categorised on the basis of their oxidation states, as this can have a significant impact on their fate and behaviour in the environment and their effects on organisms. On this basis we would expect there to be in the region of 16 categories for platinum group metals and 2 categories for rhenium. It may not be necessary to undertake environmental assessments for oxidation states which are unstable in environmental media, although the resulting oxidation state would need to be considered (this would apply for oxidation states with a reasonable worst case half-life in the environment of <12 hours). The possibility that further subgroups may be required cannot be discounted at this stage where there are marked differences in the behaviour or effects between compounds of the same oxidation state, for example if potentially toxic anions are present. A realistic estimate of the number of categories that might result from this phase of the project is therefore ~18, with an overall indicative price of ~£180000 (one hundred and eighty thousand pounds sterling; excl. VAT).

We would aim to complete this task within 12 months of the end of Phase I (i.e., 16 months after project inception), but this would depend on the volume of studies that require detailed assessment, which is currently unknown.

PHASE III: TEST PROGRAMME DESIGN

At this stage, before collation of available data and examination of potential grouping, it is not possible to define exactly what empirical testing would be required. However, we are able to state some principles that we would follow when designing and monitoring a test programme.

1. The design of the test programme would be *de minimis* and would draw extensively on arguments for test derogations in Phase II (and could also be influenced by the outcome of the risk assessments undertaken in Phase IV). It is quite possible that, on the basis of read-across or negligible exposure, no *in vivo* testing will be required for one or more categories identified in Phase II.

2. When testing does appear to be unavoidable for an endpoint within a category we will identify the minimum number of tests required to establish a valid result for that endpoint. For example, if acute invertebrate data are missing for a group we would identify members of that category with the most different physical and chemical characteristics and design tests for them in order to maximise the potential for data read-across.

3. Wherever possible, we would recommend the use of more cost-effective *in vitro* or limit tests. For example, if an acute fish test is required, but there is evidence from invertebrate tests to suggest that members of a category display similar toxicity, we would design a programme in which limit tests with fish were used to examine whether toxicity to fish was similar for just two category members with the most different physical and chemical characteristics.

4. We would use our contacts with colleagues at the EC's Joint Research Centre to test our views on *de minimis* approaches to testing, and would not commission any toxicological tests until approval has been given by the ECHA, as required under REACH.

5. We would manage the commissioning of any required studies by drawing up a detailed test programme specification, agreeing it with the PMC, and sending it to at least three GLP-compliant contract research laboratories who express an interest in tendering for the studies(s) when initially contacted by telephone. Ideally, one laboratory would be used to perform all required tests so that volume discounts can be negotiated and study monitoring is easier and therefore less expensive.

6. During the tendering process we would visit each laboratory and assess its competence to perform the required tests, using the criteria identified under ISO 17025.

7. We would provide our recommendations to the PMC Project Leader on the best value location to perform each test on the basis of competence and cost.

8. When one or more contract laboratories have been selected to perform one or more tests we would make an unannounced visit to that laboratory during a test and would monitor competence once again according to ISO 17025 criteria.

9. Finally, we would complete the Phase II matrix using the results from the testing programme, revaluate categories and produce a report for the PMC on the outcomes of the programme and their implications for REACH registration.

The overall cost of empirical testing is unknown until substance categories and data gaps have been determined. However, we estimate that if an intelligent testing approach is commissioned for a

category, based on a PGM category for which there are no hazard data, the overall indicative cost of performing, monitoring and reporting test results for two substances within each category would be:

- Ecotoxicology:
  - 1-10 tonne pa requirements = ~£23000
  - 10-100 tonne pa requirements = ~£33000
- Toxicology
  - 1-10 tonne pa requirements = ~£50000
  - 10-100 tonne pa requirements = ~£150000

We would aim to complete an initial test programme design within two months of the end of Phase II. The duration of the test programme itself will depend on the volume of tests required and the capacity and turnaround time of the contract laboratories. However, none of the required tests are of particularly long duration so this part of the programme is unlikely to take more than six months to complete if there is sufficient laboratory capacity. In any case it might be advisable not to initiate any experimental studies until at least some preliminary output from Phase IV is available. Phase III of the project would be undertaken by staff at WCA Environment limited (Mark Crane, Graham Merrington, Adam Peters, Chris Watts and Albania Grosso) and bibra (James Hopkins, Pete Watts, Philip Copestake and Tanya Diver), with study monitoring performed by a team comprising Paul Brantom (mammalian toxicology), Mark Crane (ecotoxicology) and Chris Watts (analytical chemistry). Both the latter are UKAS trained laboratory assessors.

PHASE IV: PRODUCTION OF CHEMICAL SAFETY ASSESSMENTS AND REPORTS

Chemical safety reports (CSR) must be submitted to the ECHA for substances manufactured or imported above 10 tonnes per years. For on-site isolated intermediates, dossier and substance evaluation do not apply. However the Member State Competent Authority (MSCA) where the manufacturing site is located may request additional information.

Information sent to us by the PMC show that the number of substances which fall in the >10 tonnes per year tonnage bands and are not intermediates are as follows:

- Rhenium – one substance

We would follow the guidance contained in MERAG (Fact Sheets 02, 05, 06) and HERAG (Fact Sheets 01, 02, 03) on exposure assessments for human health and the environment, in addition to relevant available regulatory guidance, when producing CSA/CSRs, particularly when considering exposure scenarios. Input would also be required from both producers and downstream users of the substances in order to develop sufficiently robust exposure scenarios.

The CSA/CSR will comply with the format and content detailed in Annex I of the REACH regulations. These require that the CSR contains the following 10 sections:

- Substance identity and physical and chemical properties
- Manufacture and uses
- Classification and labelling
- Environmental fate properties
- Human health hazard assessment

- Human health hazard assessment of physicochemical properties
- Environmental hazard assessment
- PBT and vPvB assessment
- Exposure assessment
- Risk characterisation

Derivation of DNELs and PNECs is carried out during human health and environmental hazard assessment. Exposure scenario development is the core process to carry out a Chemical Safety Assessment. The first assessment is based on the required minimum data plus all available hazard information, and on exposure estimates that correspond to initial assumptions about operating conditions and risk management measures (an initial exposure scenario). If the initial assumptions lead to a risk characterisation indicating that risks to human health and the environment are not adequately controlled then it is necessary to carry out an iterative process with amendment of one or more factors in the hazard or exposure assessment, with the aim of demonstrating adequate control. The refinement of hazard assessment may require generation of additional hazard information. The refinement of exposure assessment may involve appropriate alteration of the operational conditions or risk management measures in the exposure scenario or more precise exposure estimation. The exposure scenario, resulting from the final iteration (a final exposure scenario), is included in the Chemical Safety Report and attached to the Safety Data Sheet.

Exposure scenarios will cover any manufacture and all identified uses. In particular, an exposure scenario will include, where relevant, a description of:

- Operational conditions
  - processes involved, including the physical form in which the substance is manufactured, processed and/or used,
  - activities of workers related to the processes and the duration and frequency of their exposure to the substance,
  - activities of consumers and the duration and frequency of their exposure to the substance,
  - duration and frequency of emissions of the substance to the different environmental compartments and sewage treatment systems and dilution in the receiving environmental compartment.
- Risk management measures
  - risk management measures to reduce or avoid direct and indirect exposure of humans (including workers and consumers) and the different environmental compartments to the substance,
  - waste management measures to reduce or avoid exposure of humans and the environment to the substance during waste disposal and/or recycling.

Exposure levels will need to be estimated for each exposure scenario and for all relevant exposure routes (e.g., oral, inhalation, dermal). The exposure estimation will then be carried forward to the risk characterisation in the Chemical Safety Report and compared with the appropriate DNELs and PNECs to determine if risks to humans and the environment are adequately controlled. The CSR format will comply with that detailed in Section 7 of REACH Annex I.

The PMC has stated that compilation of IUCLID 5 files and Registration dossiers will take place in Phase V of the project, but in reality CSAs, CSRs and preparation of IUCLID 5 files will take place in parallel because they are interlinked activities. For this reason, and because we do not yet know the number of uses that would need to be included in a CSR, we cannot provide accurate prices at this stage for all possible CSAs/CSRs in this project. However, an indicative cost per CSA/CSR is in the region of £3500 to £10000 (three thousand five hundred to ten thousand pounds sterling; excl. VAT)

assuming that data collation and reviewing, robust summary preparation and IUCLID 5 entry are undertaken in other phases, and that there are a limited number of straightforward exposure scenarios.

This Phase of the project would be undertaken by staff at WCA Environment limited (Mark Crane, Graham Merrington, Adam Peters, Chris Watts and Albania Grosso) and bibra (where James Hopkins, Pete Watts, Philip Copestake and Tanya Diver will be responsible for supervision and quality of the mammalian toxicology contribution). We would aim to complete this task within twelve months of the end of Phase III.

PHASE V: COMPILATION OF IUCLID 5 FILES AND REGISTRATION DOSSIERS

Submission must be electronically via IUCLID 5 software and must contain the following information:

- Manufacturer/importer identity
- Substance identity, manufacture and use
- Tonnage band
- Substance classification and labelling
- Safe use guidance and uses advised against
- Substance intrinsic properties in the form of robust summaries
- Whether the above information has been reviewed by an assessor
- Proposals for further testing, if relevant
- Main use categories, type of uses and significant routes of exposure (for substances registered in quantities of 1 to 10 tonnes per year)

Table 1 contains the endpoints for which data are required to input into IUCLID 5 for substances which fall within the 1-10 and 10-100 tonnage bands. IUCLID 5 input will be conducted by staff with full training in use of IUCLID 5.

As before, we cannot provide accurate price estimates for this Phase until completion of Phase I. However, an indicative cost for compilation of IUCLID 5 files and Registration dossiers for each substance/category is in the region of £5000 to £10000 (five to ten thousand pounds sterling; excl. VAT) assuming that data selection is performed in other Phases and that there are not very large numbers of studies for individual IUCLID 5 entries. On average it seems likely that compiling IUCLID 5 files for substances falling into the 1-10 tpa band is likely to cost less than for substances falling into the 10-100 tpa band, because of the different data requirements. However, this depends entirely on the number of individual studies available per substance. It is quite possible that there will be large numbers of studies available for a lower tonnage band substance and very few available for a higher tonnage band substance, which would lead to a lower charge for the latter compared to the former. Costs might also be reduced if a category template is produced in IUCLID to allow a particular endpoint to be linked to dossiers for several substances within a category. A more accurate price estimate for Phase V can only reasonably be attempted after completion of Phases I and II. However, estimates for work performed in Phase V would be provided for each task and transparent records of time spent on each task would be maintained.

This Phase of the project would be undertaken by staff at WCA Environment limited (Mark Crane, Graham Merrington, Adam Peters, Chris Watts and Albania Grosso) and bibra (where James Hopkins, Pete Watts, Philip Copestake and Tanya Diver would be responsible for supervision and quality of data entry on mammalian toxicity aspects). We would aim to complete this task within twelve months of the end of Phase III, in parallel with Phase IV. If the estimated timescales in earlier Phases are not exceeded and the project begins in July 2008, the Registration dossiers for all substances would be

submitted to the PMC by July 2011. However, note that there are considerable uncertainties about test laboratory capacity, which means that testing in Phase III may not be achievable within six months. If this is the case, the project phases will need to be discussed further with the PMC to ensure that Registration takes place at a time that balances the commercial desire to Register early with the technical and regulatory requirements of REACH.

Table 1. IUCLID endpoints required for substances in 1-10 and 10-100 tonnage bands (endpoints in light red are applicable only to tonnage band 10-100 and those in dark red are for tonnage of greater than or equal to 100.

7.0.0.0	PHYS-CHEM	8.0.0.0	TOXICITY	9.0.0.0	ECOTOXICITY
7.1.0.0	Physical state	8.1.0.0	SKIN IRRITATION OR SKIN EROSION	9.1.0.0	AQUATIC TOXICITY
7.2.0.0	Melting point	8.1.0.0 (1)	Assessment of available human & animal data	9.1.1.0	Short-term Daphnia
7.3.0.0	Boiling point	8.1.0.0 (2)	Assessment of the acid or alkaline reserve	9.1.2.0	Algae
7.4.0.0	Relative density	8.1.0.0 (3)	In vitro study for skin corrosion	9.1.3.0	Short-term fish
7.5.0.0	Vapour pressure	8.1.0.0 (4)	In vitro study for skin irritation	9.1.4.0	Sludge respiration inhibition
7.6.0.0	Surface tension	8.1.1.0	In vivo skin irritation		
7.7.0.0	Water solubility	8.2.0.0	EYE IRRITATION	9.1.5.0	Long-term Daphnia
7.8.0.0	Partitioning octanol-water	8.2.0.0 (1)	Assessment of available human & animal data	9.1.6.1	FELS Fish ELS
7.9.0.0	Flash point	8.2.0.0 (2)	Assessment of the acid or alkaline reserve	9.1.6.2	Fish Embryo
7.10.0.0	Flammability	8.2.0.0 (3)	In vitro study for eye irritation	9.1.6.3	Fish Juvenile Growth
7.11.0.0	Explosive properties	8.2.1.0	In vivo eye irritation	9.2.0.0	DEGRADATION
7.12.0.0	Self ignition temperature	8.3.0.0	SKIN SENSITISATION	9.2.1.1	Ready biodegradation
7.13.0.0	Oxidizing properties	8.3.0.0 (1)	Assessment of the available human, animal & alternative data	9.2.1.2	Simulation test water
7.14.0.0	Granulometry	8.3.0.0 (2)	In vivo testing	9.2.1.3	Simulation test soil
7.15.0.0	Stability of substance	8.4.0.0	MUTAGENICITY	9.2.1.4	Simulation test sediment
7.16.0.0	pKa	8.4.1.0	In vitro gene mutation study in bacteria		
7.17.0.0	Viscosity	8.4.2.0	In vitro cytogenicity study in mammalian cells or in vitro micronucleus test	9.2.2.1	Hydrolysis
				9.2.3.0	Identif. Deg. Products
		8.4.3.0	In vitro gene mutation study in mammalian cells	9.3.0.0	FATE & BEHAVIOUR
		8.5.0.0	ACUTE TOXICITY	9.3.1.0	Ads/Des Screening
		8.5.1.0	By oral route	9.3.2.0	Bioaccumulation in fish
		8.5.2.0	By inhalation route		
		8.5.3.0	By dermal route	9.3.3.0	Further info on adsorp/desorp
		8.6.0.0	REPEATED DOSE TOXICITY		
		8.6.1.0	Short-term repeated dose toxicity study (28 days)		
		8.6.2.0	Subchronic toxicity study (90 days)		
		8.7.0.0	REPRODUCTIVE TOXICITY		
		8.7.1.0	Screening for reproductive/developmental toxicity (OECD 421 or 422)		
		8.8.0.0	TOXICOKINETICS		
		8.8.1.0	Assessment of toxicokinetic behaviour from available information		
		8.7.2.0	Pre-natal developmental toxicity study (e.g. OECD 414)		
		8.7.3.0	Two-generation reproductive toxicity study		

Expertise

We have assembled a project team comprising Dr Mark Crane (Project Manager and Key Account Manager), Albania Grosso, Dr Graham Merrington, Dr Adam Peters, and Dr Chris Watts (all WCA), James Hopkins, Pete Watts, Philip Copestake and Tanya Diver (all bibra), and Dr Paul Brantom (Brantom Risk Assessment - who would organise, monitor and assess any required Phase III mammalian toxicity studies). Pen portraits for these staff are provided below and full curricula vitae for all of them are in Appendix 1. This team provides high level expertise in the fate, behaviour, environmental toxicology, mammalian toxicology and risk assessment of metals.

Mark Crane, PhD, is a Director at WCA Environment and an environmental toxicologist with over 20 years of experience in environmental consultancy and academia. Mark will lead and manage the project and has extensive experience in assessing ecotoxicology data for government and commercial clients for the OECD HPV programme and under the Existing Substances Regulations. He is currently project manager for a UK Defra contract to review the environmental parts of all SIARs passing through the SIAM process.

Albania Grosso, MSc, is a Principal Scientist at WCA Environment and an environmental scientist with over 14 years experience in environmental consultancy and environmental regulation. Albania has extensive expertise in chemical exposure assessment and has provided advice to UK regulators and EU committees. She has expertise in assessing the fate and behaviour of substances in the environment for both human and ecological receptors.

Graham Merrington, PhD is a Director at WCA Environment and an environmental scientist with over 14 years of experience in environmental consultancy, environmental regulation and academia. He represented the UK at Expert Groups for the Water Framework Directive, and was a regular attendee as an expert for metals-related issues at European Commission TCNES. He has considerable experience in the environmental risk assessment of trace metals and has been closely involved in the Existing Substances Regulations metals risk assessments, in the development of Environmental Quality Standards for metals and the preparation of the Metals Environmental Risk Assessment Guidance (MERAG). Graham has recently worked with regulatory colleagues on REACH Implementation Project Expert Working Groups to define appropriate ecotoxicity testing approaches under the REACH regulations. His main areas of expertise are in the assessment of environmental fate and behaviour of chemicals; soil chemistry and chemical bioavailability; bioaccumulation and biomagnification through food chains; environmental management frameworks; and project management.

Adam Peters, PhD is a Principal Scientist at WCA Environment and an environmental chemist with over 9 years of experience in environmental consultancy, environmental regulation and academia. He has been responsible for management of environmental aspects of the Notification of New Substances scheme and the Existing Substances Regulations in the UK, and has recently been a regular attendee as an expert for metals-related issues at European Commission TCNES. He has been closely involved with the development of Environmental Quality Standards for metals and the preparation of the Metals Environmental Risk Assessment Guidance (MERAG). Adam's main areas of expertise are in the assessment of environmental fate, behaviour, bioavailability and effects of trace metals; environmental risk assessment of industrial chemicals; assessment of persistent, bioaccumulative and toxic (PBT) substances; Hazard assessment of waste materials and their recovery; and development and validation of environmental quality standards.

Chris Watts, PhD is a Director at WCA Environment and an environmental chemist with over 30 years of experience in environmental research and consultancy. He is a member of the Royal Society of Chemistry and is currently chairman of the RSC's Water Science Forum Committee. He is also a member of the RSC's Energy, Sustainability and Environment Forum and has served on BSi and ISO environmental standards committees and on Defra's Shadow Health Advisory Group for Chemical Contamination Incidents. Chris also has extensive expertise in applying existing approaches and models for environmental risk assessment (ERA) of chemicals, assessment of the environmental behaviour, fate and effects of chemicals and designing implementing environmental monitoring programmes.

Staff at WCA Environment are well placed to provide advice and services to the precious metals industry because of our familiarity with the European chemicals management regulations and specific knowledge of the difficulties in assessing metals and metal compounds.

James Hopkins is a toxicologist at bibra with 32 years of experience in the field of chemical toxicology. He managed a sizeable group of desk-based toxicologists in a research organisation for many years and, since 2003, has been Managing Director of a company providing high-quality consultancy and advice to industrial organisations and government departments on all aspects of chemical toxicology. He has extensive experience in reviewing and critically evaluating toxicological data for a wide range of chemicals and a cross-section of industrial sectors. James has also been involved in compiling a large number of critical reviews of chemicals and several strategy documents for national governments on both sides of the Atlantic. James is on the Register of Toxicologists of EUROTOX and of the Institute of Biology/British Toxicology Society.

Peter Watts has specialized in chemical toxicology at bibra since 1981. Peter has been involved in a number of different European projects including EU-funded Concerted Action Projects instigated to construct EUROPOEM, a generic databases of operator, bystander and re-entry worker exposures to plant protection products and to develop predictive models, and RIP3.3-1, a scoping project aimed at producing guidance for data requirements under REACH, including consideration of data sources, data quality, alternatives to study data and study waivers. He has also authored or co-authored a number of WHO-IPCS CICADs and has acted as a temporary adviser to the WHO at FRB meetings where the CICADs have been finalized. Peter has many years experience of reviewing and critically evaluating toxicological data on a wide range of chemicals for government departments and industrial organisations. Peter is on the Register of Toxicologists of EUROTOX and of the Institute of Biology/British Toxicology Society.

Philip Copestake is a toxicologist at bibra with over 20 years experience. He has authored or co-authored a number of WHO-IPCS CICADs and has acted as a temporary adviser to the WHO at FRB meetings where the CICADs have been finalized. He was involved, from 1991-2000, in the production of the International Chemical Safety Cards (ICSCs), a project co-ordinated by the International Programme on Chemical Safety of the WHO, and served as a member of the Peer-Review Committee for this project. Philip's background in Information Sciences has led to him giving a number of external presentations and lectures on the use of information resources in toxicology, at the University of Surrey. He is experienced in reviewing and critically evaluating toxicological data on a wide range of chemicals and has considerable knowledge of the preparation of dossiers for submission to regulatory authorities. Philip is on the Register of Toxicologists of EUROTOX and of the Institute of Biology/British Toxicology Society.

Tanya Diver is a toxicologist at bibra with over 22 years of experience in reviewing and critically evaluating toxicological data on a wide range of chemicals. She is an experienced writer and peer-reviewer of literature reviews, and has prepared numerous independent hazard and risk assessments

of chemicals for both industry and government departments around the world. She is the author of over fifty bibra Toxicity Profiles, and contributes regularly to the bibra monthly current-awareness journal, *Toxicology and Regulatory News*. Tanya is on the Register of Toxicologists of EUROTOX and of the Institute of Biology/British Toxicology Society.

Bibra – toxicology advice & consulting staff are well suited to provide advice and services to the precious metals industry because of their expertise in chemical toxicology and the unique toxicology database and databank which allows them instant access to critical toxicity data.

Paul Brantom, PhD is the principal of Brantom Risk Assessment Ltd. Paul has worked in the field of toxicology for more than 34 years, combining experience of supervising the conduct of all varieties of experimental regulatory toxicology studies to GLP and consultancy support to a variety of organisations and companies. Particular interests are the use of in vitro models in risk assessment as well as quantitative toxicological risk assessment. He joined BIBRA in 1969 and until March 2004 was Head of Toxicology and Information Services at BIBRA International. Paul managed the Centre for Toxicology at the University of Surrey, Guildford, for more than 3 years and has retained links with the Centre. The Centre is conceived to bring focus to the toxicological activities of the School of Biomedical and Life sciences and runs a very popular course for managers in the fundamentals of toxicology. As a registered European Toxicologist Paul has worked for numerous companies and organisations in various capacities relating to toxicological evaluation and registration of products. He is currently a member of the UK Veterinary Products Committee(VPC), Veterinary Residues Committee (VRC), Advisory Committee on Animal Feedingstuffs (ACAF), Advisory Committee on Novel Foods and Processes (ACNFP) and the European Food Safety Authority (EFSA) Panel on Additives to Animal Feed (FEEDAP).

Project management and Quality Assurance

Mark Crane will be overall Project Executive with responsibility for ensuring overall project delivery to time, quality and budget. Albania Grosso will be Project Manager with responsibility for daily project administration. She will proactively liaise with all project staff at WCA and bibra and will organise and minute monthly teleconferences between PMC representatives and relevant project staff.

WCA Environment is accredited to ISO 9001 and will manage the project within that quality system. All outputs will be peer reviewed by at least one other member of the project team before being submitted to the PMC. WCA Environment also operates an Environmental Management System accredited to ISO 14001.

Financial offer

The prices quoted below are firm for Phase I and indicative for subsequent phases. All prices are quoted in pounds sterling, excluding any applicable VAT, and are valid until 30 June 2008.

Phase	Cost
Phase 1: Literature Search and Data gap analysis	
Rhenium (option 1)	1550
Rhenium (option 2/3)	1100
Phase II: Test Derogation Assessment	
Rhenium (likely to be up to 2 categories)	£10000 per substance/category
Phase III: Test Programme Design (estimated prices for testing two substances per category	
Rhenium	
Ecotox (1-10 tonnes)	£23000
Ecotox (10-100 tonnes)	£33000
Mammalian Toxicology (1-10 tonnes)	£50000
Mammalian Toxicology (10-100 tonnes)	£150000
Phase IV: Production of CSA/CSR	
Rhenium	£3500-£10000 per substance/category
Phase V: IUCLID 5 Files and Registration Dossiers	
Rhenium	£5000-£10000 per substance/category