

Our Ref: SC210001

Your Ref:

Date: 09/07/2021

Dear Sirs/Madams,

**Contract Ref: SC210001**

**Contract Title: Toxicological advice on air pollutants**

You are invited to quote for the above in accordance with the enclosed documents.

Instructions on what information we require you to provide is in Section 4 of the following Request for Quotation document.

Your response should be returned to the following email address by 17:30 on 2/8/2021.

ian.martin@environment-agency.gov.uk

Please confirm, by email, whether you intend to submit a quote as we may wish to update you with additional information during the quotation period.

If you have any queries, please do not hesitate to contact me.

Yours sincerely

Ian Martin

Senior Specialist (Land team), Chief Scientist’s Group

E-mail: ian.martin@environment-agency.gov.uk

Telephone: 07770 334935

**The Environment Agency**, Aqua House, Lionel Street, Birmingham B3 1AQ

**Request for Quotation**

**Ref: SC210001**

**Title: Toxicological advice on air pollutants**

**Section 1**

**Who is the Environment Agency?**

We are an Executive Non-departmental Public Body responsible to the Secretary of State for Environment, Food and Rural Affairs. Our principal aims are to protect and improve the environment, and to promote sustainable development.

Further information on our responsibilities, Corporate Plan and how we are structured can be found on our Website.

<https://www.gov.uk/government/organisations/environment-agency/about>

**What do we spend our money on?**

We are a major procurer of goods and services within the UK, spending circa £600M per annum, our major spend areas are:

* Flood and Coastal Risk Management (design, construction and maintenance)
* ICT and Telecommunications
* Vehicles and Plant
* Environmental Consultancy and Monitoring
* Temporary Staff and Contractors
* Facilities Management, Energy and Utilities
* Flood Management and Water Related Services

**What do we need from our suppliers?**

Suppliers are vital in supporting the delivery of our corporate plan. We aim to support the economy and society whilst delivering more environmental outcomes for every pound we spend. In many areas we are leading the way on environmental and technical developments. It is our role to ensure that suppliers clearly understand our corporate aims and objectives and know that we are committed to delivering the best value most sustainable solutions, taking into account the whole life cost of our procurement decisions. We promote diversity and equality and treat all of our suppliers fairly.

Our procurement strategy may be of interest to you as a potential supplier. It sets out our priorities and key commitments in a range of areas such as delivering our corporate plan, Government policy, supplier management and sustainable procurement:

<https://www.gov.uk/government/organisations/environment-agency/about/procurement#procurement-strategy>

**Government changes and collaboration**

Since 1 April 2013, the Environment Agency is no longer responsible for delivering the environmental priorities of Wales. This is now the remit of Natural Resources Wales (NRW).Further information can be found here:

<http://naturalresources.wales/splash?orig=/>

By bidding for this requirement, you may also be approached by other members of the Defra network, NRW or other government departments that are specifically named in the tender document.

**Further information**

For further information and to see our commitments to Diversity and Equality, please visit our website.

<https://www.gov.uk/government/organisations/environment-agency/about/procurement>

https://www.gov.uk/government/organisations/environment-agency/about/equality-and-diversity

Also, are you up to date on environmental legislation? See links below for further information.

Waste and Environmental Impact - <https://www.gov.uk/browse/business/waste-environment>

Environmental Regulations - <https://www.gov.uk/browse/business/waste-environment/environmental-regulations>’

**Section 2**

**The Customer**

**Summary**

This work is being commissioned by the Research team within the Chief Scientist’s Group. The work of the Environment Agency’s Chief Scientist’s Group is a key ingredient in the partnership between research, guidance and operations that enables the Environment Agency to protect and restore our environment. The team focuses on four main areas of activity:

* Setting the agenda, by providing the evidence for decisions;
* Maintaining scientific credibility, by ensuring that our programmes and projects are fit for purpose and executed according to international standards;
* Carrying out research, either by contracting it out to research organisations and consultancies or by doing it ourselves;
* Delivering information, advice, tools and techniques, by making appropriate products available.

## Contract Length

It is anticipated that this contract will be awarded to one supplier for a period of 7 months to end no later than 31/03/2022. Prices will remain fixed for the duration of the contract award period. We may at our sole discretion extend this contract to include related or further work. Any extension shall be agreed in advance of any work commencing and may be subject to further competition. Any amendment to contract prices for the extensions are to be by negotiation.

The Environment Agency Conditions of Contract for Research (Appendix C) shall apply to this contract.

This contract shall be managed on behalf of the Agency byIan Martin, ian.martin@environment-agency.gov.uk.

## Contact Details and Timeline

Ian Martin will be your contact for any questions linked to the content of the quote pack or the process. Please submit any questions by email and note that both the question and the response will be circulated to all tenderers that have previously confirmed by email their intention to submit a quotation.

Key elements of the process have been reviewed. Anticipated dates for planned activities are below:

|  |  |
| --- | --- |
| **Activity** | **Due Date** |
| Supplier responses for Request for Quote | 02/08/2021 17:30 |
| Evaluation of Request for Quote submissions | 06/08/2021 |
| Award of contract | 01/09/2021 |
| Project/Contract end date | 31/03/2022 |

It should be noted that these timescales and activities may be subject to change.

**Section 3**

## Evaluation Criteria

We will award this contract in line with the most economically advantageous tender (MEAT) as set out in the following award criteria:

* Price – 60%
* Quality – 40%

The following quality criteria are weighted in accordance with the importance and relevance attached to each one.

|  |  |
| --- | --- |
| Experience of reviewing and summarising mammalian and human toxicology of chemicals  | 35% |
| Adequacy of staff resources (including for project management) | 35% |
| Project methodology (including project management oversight) | 10% |
| Ability to deliver a successful project to time and budget | 20% |

The criteria listed above will be assessed on a 0 to 10 basis and will reflect the following judgements:

|  |  |
| --- | --- |
| **Rating of Response****The tenderer provides a response which in the opinion of the evaluators is:**  | **Score** |
| **Excellent:** Addresses all of the requirements and provides a response with relevant supporting information which does not contain any weaknesses, giving the Agency complete confidence that the requirements will be met. | 10 |
| **Very Good:** Addresses all of the requirements and provides a response with relevant supporting information, which contains very minor weaknesses, giving the Agency high confidence that the requirements will be met. | 8 |
| **Good:** Addresses all of the requirements and provides a response with relevant supporting information, which contains minor weaknesses, giving the Agency reasonable confidence that the requirements will be met.  | 6 |
| **Satisfactory:** Substantially addresses the requirements and provides a response with relevant supporting information which may contain moderate weaknesses, but gives the Agency some confidence that the requirements will be met.  | 4 |
| **Weak:** Partially addresses the requirements, or provides supporting information that is of limited relevance or contains significant weaknesses, and therefore gives the Agency low confidence that the requirements will be met. | 2 |
| **Nil:** No response or provides a response that gives the Agency no confidence that the requirements will be met.   | 0 |

**Section 4**

**Information to be returned**

**Please note, the following information requested must be provided. Incomplete tender submissions may be discounted.**

Please complete and return the following information:

* details of the personnel you are proposing to carry out the service, including CV’s of your key personnel;
* detail your recent experience of carrying out similar contracts or projects
* details of proposed methodology
* completed Pricing Schedule (Appendix A);
* completed Prior Rights Schedule (Appendix B);
* confirmation that terms and conditions are accepted (Appendix C. Please note that the terms cannot be amended later).

**Section 5**

**Specification**

# Background to the Requirement

The Environment Agency (EA) regulates chemical emissions from industrial and waste management activities under the Environmental Permitting Regulations 2016 (EPR). Horizontal Guidance document H1 is the principal guidance on environmental risk assessment for new permit applications. Applicants use H1 to identify and manage significant emissions that could impact public health and the environment.

In assessing risks to health, H1 recommends that predicted emissions are screened against Environmental Assessment Levels (EALs) for the chemicals of concern. EALs are defined as air concentrations indicative of non-appreciable or minimal concern to health from short- or long-term inhalation exposure. They cover about 90 substances including industrial chemicals and classical air pollutants. Many EALs are based on withdrawn occupational exposure limits and were last reviewed in detail in the early 2000s.

The EA published its current methodology for the derivation of EALs in 2012 with a greater emphasis on a robust review of the scientific evidence on adverse health effects. Working in partnership with Public Health England (PHE), the EA initiated a systematic review of EALs in 2019 to ensure that the existing recommendations are underpinned by the latest science. As a result, the EA has recently completed external consultation on revised EALs for 12 substances including two new substances identified as being critical to the regulation of the carbon capture sector.

**References**

**List of Environmental Assessment Levels**

<https://www.gov.uk/guidance/air-emissions-risk-assessment-for-your-environmental-permit#environmental-standards-for-air-emissions>

**Guidance on the Derivation of Environmental Assessment Levels**

<https://www.gov.uk/government/consultations/derivation-of-new-environmental-assessment-levels-to-air>

**Consultation on New Environmental Assessment Levels (Nov 2020 to Feb 2021)**

<https://consult.environment-agency.gov.uk/environment-and-business/new-air-environmental-assessment-levels/>

# Specific Objectives/Deliverables

The main objective of this project is to provide specialist consultancy advice on human and mammalian toxicology to enable the EA and PHE to continue the on-going review and revision of EALs. It will include the production of quick scoping reviews (QSR) on the toxicology of specific chemicals from the open and grey scientific literature (the QSR dossier for monoethanolamine is provided as an example in Appendix D). In addition, the contractors may be required to provide expert advice on request, in the form of a briefing note, for selected toxicological issues such as a synthesis of *in vitro* and *in vivo* evidence on genotoxicity and mutagenicity. The work undertaken will be carried out under the direction of the Chief Scientist’s Group, who will also liaise with PHE.

Key activities:

1. Revise a number of draft chemical dossiers (see Table 1) to address evidence gaps. The tasks associated with each dossier will vary but broadly include:
	1. Revise the drafts to take into account information from oral studies reported in authoritative reviews for short- and long-term exposures and make recommendations for route-to-route extrapolation in the absence of sufficient evidence on inhalation exposures
	2. Revise the drafts to take into account specific limitations identified (for example, the genotoxicity and mutagenicity status of chloromethane) following a critical review of the primary open and grey literature on human and mammalian toxicology
	3. Work with EA and PHE to finalise the dossiers and incorporate the reasoning for the recommended EAL

1. Revise the prioritisation of outstanding substances for review from the published list of EALs based on their current relevance (for example, through the Pollution Inventory), a screening assessment of their relative hazard, and the availability of updated authoritative opinions and the primary toxicological literature.

1. Prepare new chemical dossiers in accordance with the published methodology and using the existing dossiers as a guide. Address any questions that arise from review by EA and PHE, and revise the dossiers based on recommended EALs. The list and number of substances to be addressed will depend on the prioritisation exercise, available budget, and timescales.

Table 1 Chemicals with an existing draft and the areas that will be finalised under this contract

|  |  |  |  |
| --- | --- | --- | --- |
| **Substance** | **Short-term EAL** | **Long-term EAL** | **Other issues** |
| Butadiene | Yes |  |  |
| Carbon tetrachloride | Yes | Yes |  |
| Chloromethane |  |  | Mutagenicity |
| Copper dust/mist |  | Yes | Oral studies |
| Dichloromethane | Yes | Yes |  |
| Hydrogen cyanide | Yes | Yes |  |
| Mercury |  | Yes | Oral studies |
| Selenium |  | Yes | Oral studies |
| 1,2,4-trichlorobenzene |  |  |  |
| Zinc oxide | Yes | Yes | Oral studies |

Key requirements:

* The supplier will have specialist experience of the synthesis and critical evaluation of mammalian and human toxicology and be able to summarise key studies and decisions effectively and succinctly.
* A single point of contact will be provided by the supplier.
* Deliverables and timescales are outlined below.

### Timescales/Deadlines

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Task No. | Deliverable | Responsible party | Format / Compatibility Requirements | Date of completion, end: |
| 1 | **Start-up meeting** with project team and the EA steering group, confirming:* Dossiers to be revised
* Approach to review of prioritisation
* Project deliverables and timings
 | Supplier | MS Teams meeting/ Telecon | 10 Sep 2021 |
| 2 | **Draft revised dossiers** in Table 1 to EA (these can be provided in batches) | Supplier  | Word documents | 29 Oct 2021 |
| 3 | EA steering group reviews report and provides **comments** back to project team | EA project manager | Track changes in word document | 12 Nov 2021 |
| 4 | **Final revised dossiers** | Supplier | Word documents | 3 Dec 2021 |
| 3 | **Draft prioritisation report** to EA | Supplier | Word document | 3 Dec 2021 |
| 4 | EA steering group reviews prioritisation and provides **comments** back to project team | EA project manager | Track changes in word document | 17 Dec 2021 |
| 5 | **Final prioritisation report** to EA | Supplier | Word document | 7 Jan 2022 |
| 6 | **Progress meeting** with project team and the EA steering group, confirming:* Final prioritisation
* Programme for new dossiers
 | Supplier | MS Teams meeting/ Telecon | 7 Jan 2022 |
| 7 | **Draft new dossiers** to EA (these can be provided in batches but all drafts must be submitted by the task end date) | Supplier | Word documents | 3 Mar 2022 |
| 8 | EA steering group reviews report and provides **comments** back to project team (end date based on receipt of final drafts) | EA project manager | Track changes in word document | 17 Mar 2022 |
| 9 | **Final revised dossiers** | Supplier | Word documents | 31 Mar 2022 |

### Skills of Personnel Required

# Technical expertise in mammalian and human toxicology including critical evaluation of primary open and grey literature on a range of industrial contaminants.

# Excellent communication skills (written, pictorial and verbal).

# Ability to work collaboratively and share knowledge.

**Section 6**

**Contract Management**

This contract shall be managed on behalf of the Agency byIan Martin, ian.martin@environment-agency.gov.uk

The contractor is required to maintain close liaison with the Environment Agency's Project Manager.

During the course of the project, the contractor will provide the Environment Agency’s Project Manager with regular updates (monthly or fortnightly) regarding:

* progress and difficulties encountered with the project
* any proposed changes to the manner in which the project is run
* time spent on the project
* details of the financial spend during the previous month.

An Environment Agency project steering group will be set up to act as the technical quality review panel for the work and outputs. This panel will include representation from PHE, who will provide an authoritative and independent peer review of the documents produced. Working closely with PHE is an essential part of this project. The project advisory group will review drafts produced by the contractor, prior to acceptance. You should ensure that sufficient time is allowed within the project to consult with the project steering group in directing the project. Approximately 2 weeks has been built into the schedule to allow review of draft documents.

The contractor should allow enough time for project meetings to discuss progress and agree future scope. There will be two full project meetings, both of which will be virtual and half days (3-4 hours); one at the start-up of the project and one to discuss the prioritised list of substances and agree the work schedule for the remainder of the project. Other project meetings and any other discussions needed, including project closure, will be conducted where necessary.

We will raise purchase orders to cover the cost of the services and will issue to the awarded supplier following contract award.

Before the invoice is issued, a fee note must be emailed in advance to the contract manager for approval. All invoices must quote the purchase order number in order to be processed. A file copy invoice must be provided to the contract manager, on request. The timescale for payment of invoices will be up to 30 days after we have received a valid invoice.

It is proposed that full payment be made on acceptance of the final dossiers for new substances at the end of March 2022. Alternative programmes of work and payment schedules will be considered.

**Section 7**

**Sustainability Considerations**

We are committed to continually improving our sustainability performance. The Environment Agency has set itself tough objectives as a clear commitment and contribution to sustainable development throughout England. The Agency recognises that this can only be achieved through commitment from all sectors of society and it is intent on raising awareness amongst industry and commerce.

Contractors must adopt a sound proactive environmental approach, designed to minimise harm to the environment.

Environmental criteria should be considered as part of your tender submission with credit given for innovation. Factors to be considered could include areas such as:

* + - Paper use: All documents and reports prepared by consultants and contractors are produced wherever possible on recycled paper containing at least 100% post-consumer waste and printed double sided.
		- Travel: use of public transport, reduce face to face meetings by using email and videoconferencing. Meetings to be held in locations to minimise travel and close to public transport links.
		- Packaging: should be kept to a minimum. Re-use and disposal issues must be considered.
		- Efficient Energy and Water Use.
		- Disposal of Waste: Whilst on site the contractor is responsible for the disposal of their own waste and can only use client facilities with express permission from the on-site facilities officer.
		- Whilst on site, contractors should comply with the local environmental policy statement which will be made available to you in advance or on arrival.

**Diversity and Equal Opportunities**

We are committed to promoting equality and diversity in all we do and valuing the diversity of our workforce, customers and communities.  As a public body, we publish regular information about what our equality objectives are and how we’re meeting them.

<https://www.gov.uk/government/organisations/environment-agency/about/equality-and-diversity>

**Health and Safety**

Contractors will be responsible for making sure all required health and safety aspects including risk assessments are undertaken and required management measures are in place to protect worker exposure. This includes management of all partners, consortium members and subcontractors.

**IEM2020:**

## Sustainability Objectives

As the Environment Agency, our overarching aim is to protect and improve the environment for people and wildlife. Over the last 10 years we have achieved significant reductions in our environmental impacts that occur through our everyday operations. This included a 40% reduction in our carbon emissions and a 37% reduction in the number of miles we travel. This year we have launched our new Internal Environmental Management strategy to take us through to 2020, building on these successes and widening our ambition.

**Supply chain**

Our 2020 approach will have a very strong emphasis on the indirect impacts of our supply chain.

Our supply chain accounts for over 70% of our total environmental impacts.

Working with our supply chain we want to be world class in the area of environmental management. The environmental impacts of our work and that delivered by and through our supply chain must be reduced; environmental risks must be effectively managed and opportunities for enhancements investigated.

As an organisation, our environmental management system (EMS) is accredited to ISO14001 and EMAS standards. Our procurement activities form part of this system; driving environmental performance improvements across the value chain.

## Section 8

### Additional Information

### Copyright and confidentiality

Unless otherwise indicated, the copyright in all of the documentation belongs to the Environment Agency, and the documentation is to be returned to us with your tender. The contents of the documentation must be held in confidence by you and not disclosed to any third party other than is strictly necessary for the purposes of submitting your quote. You must also ensure that a similar obligation of confidentiality is placed upon any third party to whom you may need to disclose any of the documentation for the purposes of the tender.

### Accuracy of documentation

You should check all documentation; should any part be found to be missing or unclear you should immediately contact us at the address given in the covering letter. No liability will be accepted by the Environment Agency for any omission or errors in the documentation which could have been identified by you.

### Amendments to documentation

Prior to the date for return of tenders, we may clarify, amend or add to the documentation. A copy of each instruction will be issued to every Tenderer and shall form part of the documentation. No amendment shall be made to the documentation unless it is the subject of an instruction. The Tenderer shall promptly acknowledge receipt of such instructions.

### Alternative Offers

Alternative offers may be considered if they constitute a fully priced alternative and are submitted in addition to a quotation complying with the requirements of the Invitation to Quote Documents. If, for any reason you wish to submit an alternative offer without a fully compliant tender please contact us in accordance with the details in the covering letter.

## Continuity of personnel

The Contractor shall employ sufficient staff to ensure that the Services are provided at all times and in all respects to the Project Standard. It shall be the duty of the Contractor to ensure that a sufficient reserve of staff is available to ensure project delivery in the event of staff holidays, sickness or voluntary absence

The Environment Agency will be notified immediately of any changes to personnel associated with the project. The Contractor will ensure that every effort is made to replace outgoing staff with personnel of equal calibre and expertise. All new members of staff undertaking work for the Project will need to be agreed by the Environment Agency prior to commencement.

At all times, the Contractor shall only employ in the execution and superintendence of the Contract persons who are suitable and appropriately skilled and experienced.

## Intellectual property rights

All results, including material and tools produced, developed or paid for under this contract shall be the property of the Environment Agency.

## References

The Environment Agency may request recent and relevant references prior to the award of the project.

**Contract award**

This Request for Quote is issued in good faith but we reserve the right not to award any or all of this work.

### DATA PROTECTION ACT ADDENDUM TO SPECIFICATION

## Protection of personal data

In order to comply with the Data Protection Act 1998 the Contractor must agree to the following:

* You must only process the personal data in strict accordance with instructions from the Environment Agency.
* You must ensure that all the personal data that we disclose to you or you collect on our behalf under this agreement are kept confidential.
* You must take reasonable steps to ensure the reliability of employees who have access to personal data.
* Only employees who may be required to assist in meeting the obligations under this agreement may have access to the personal data.
* Any disclosure of personal data must be made in confidence and extend only so far as that which is specifically necessary for the purposes of this agreement.
* You must ensure that there are appropriate security measures in place to safeguard against any unauthorised access or unlawful processing or accidental loss, destruction or damage or disclosure of the personal data.
* On termination of this agreement, for whatever reason, the personal data must be returned to us promptly and safely, together with all copies in your possession or control.

# APPENDIX A - PRICING SCHEDULE

ALL COSTS QUOTED MUST BE EXCLUSIVE OF VAT

All costs must be quoted on this schedule. Any costs not detailed will not be paid.

Task 7 is for the provision of new dossiers for an undefined number of substances. You should provide a day rate for all staff that may work on a dossier. You should provide sufficient information to enable us to make a comparison of indicative costs for this item on a time and materials basis for a simple dossier (for example, monoethanolamine) and a potentially more complicated dossier (for example, selenium, copper or zinc oxide).

Please detail your task costs in the table below.

|  |
| --- |
| **Cost Proposal (To be completed by Supplier)** |
| **Tasks** | **Hourly Rate** | **No of Hours** | **Cost** |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
| Total Staff Costs  |  |
| **Expenses (please detail type, i.e. travel etc)** |  |
| **Discounts applied (please detail)** |  |
| **Total Overall Cost**  |  |

**Other costs**

Please state any other costs that will need to be taken into consideration.

|  |  |
| --- | --- |
| **DESCRIPTION** | **COST** £ |
| **1. Other costs (please detail)** |  |
| **2. Other costs (please detail)** |  |
| **3. Other costs (please detail)** |  |
| **TOTAL**  |  |

**Discounts, rebates and reductions**

Please detail below any discounts, rebates and other reductions you are prepared to offer and the basis of those incentives

|  |  |
| --- | --- |
| **DESCRIPTION** | **AMOUNT**£ |
|  |  |
|  |  |
|  |  |
| **TOTAL**  |  |

**Total Overall Cost**

Please detail the total fixed cost for the project

|  |  |
| --- | --- |
| **ITEM** | **TOTAL AMOUNT**£ |
| **Staff Costs** |  |
| **Other Costs** |  |
| **Discounts/reductions** |  |
| **TOTAL Overall Cost** |  |

The following limits will be applicable to all claims for travel and subsistence under this contract:

1. Travel by rail: standard class should be used at all times
2. Travel by car: 45 pence/mile

Hotel bookings should be made through the Environment Agency’s corporate travel contract. Details of this contract are available from the Corporate Contracting Team.

When making reservations you should state that you are a contractor working on Environment Agency business.

Hotel charges must not exceed a maximum limit per night bed and breakfast (VAT included) of: £140 in London; £100 in Bristol; £90 in Warrington; £85 in Reading; £75 in Aberdeen, Birmingham, Belfast, Cardiff, Coventry, Edinburgh, Glasgow, Harlow, Leeds, Manchester, Middlesbrough, Newcastle, Oxford, Portsmouth, Sheffield and York; and £70 in all other destinations. Please note that these hotel ceiling rates are subject to change throughout the life of the contract.

Expenditure on dinner during an overnight stay must not exceed a maximum limit of £25, including a drink.

Receipts for all rail travel, hotel and food expenses will be required as proof of expenditure and will be reimbursed at cost. No profit or additional cost shall be applied by the contractor to such personal expenses.

**APPENDIX B - PRIOR RIGHTS SCHEDULE**

Details of Prior Rights held by the Parties (To be updated as Rights are introduced during the period of the Contract)

Prior Rights owned or lawfully used by a Party, whether under licence or otherwise, which it introduces to the Project for the purposes of fulfilling its obligations under the Contract.

Held by the Environment Agency

|  |  |  |
| --- | --- | --- |
| **Name and description of Prior Rights** | **Extent of proposed use in the Project**  | **Proprietary owner of the Prior Rights** |
|  |  |  |
|  |  |  |
|  |  |  |

Held by the Contractor

|  |  |  |
| --- | --- | --- |
| **Name and description of Prior Rights** | **Extent of proposed use in the Project**  | **Proprietary owner of the Prior Rights** |
|  |  |  |
|  |  |  |
|  |  |  |

**Explanation of Contractor's Prior Rights**
All Intellectual Property Rights owned by or lawfully used by the Contractor, whether under licence or otherwise before the date of this Contract. It can also mean any invention and know how or other intellectual property (whether or not patentable) owned by one of the parties prior to the commencement of the Project, or devised or discovered by one of them only in the course of other projects during the Project period and not arising directly from the Project.

**APPENDIX C – ACCEPTANCE OF TERMS AND CONDITIONS**

I/We accept in full the terms and conditions named in Section 2 and appended to this Request for Quote document.

Company \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Name

Signature \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Print Name \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Position \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**APPENDIX D – EXAMPLE QSR DOSSIER**

## Mono-ethanolamine (CAS Number 141-43-5)

MEA – also known as 2-aminoethanol, or ethanolamine – is a colourless, viscous liquid with an ammoniacal odour (HSE 2016), whose vapour is denser than air. It is widely used in industry in the production of detergents and soaps, dyestuffs, rubber vulcanisation, and as a scrubber for acidic gases in enclosed atmospheres such as submarines. MEA is used in a range of consumer products including cosmetics and personal care products, washing and cleaning products, coating products, biocides, inks and toners, and adhesives and sealants. It is rapidly biodegradable in the environment and has an estimated phototransformation half-life in air of about 11 hours (HSE 2016).

### Regulatory Standards

|  |  |
| --- | --- |
| None |  |

### Recommended Environmental Assessment Level in Air

|  |  |
| --- | --- |
| Long-term EAL | 0.1 mg/m3 as a 24-hour mean |
| Short-term EAL | 0.4 mg/m3 as a 1-hour mean |

### Overview

There are few authoritative reviews on the adverse effects from exposure to MEA (CNESST 2019, HSE 2016, SCOEL 1996). It is a strong respiratory, ocular and skin irritant. CNESST (2019) concluded that MEA is a skin and respiratory sensitiser, but this opinion has been disputed (HSE 2001 and 2016).

#### **Toxicokinetics**

Although MEA is a normal component of the human diet, part of the membrane-constituting class of glycerophospholipids and a degradation product of the amino acid serine, there is no quantitative information on its systemic uptake via the oral or inhalation routes (HSE 2016). SCOEL (1996) concluded that MEA is absorbed through the skin, lungs and gastrointestinal tract.

MEA is rapidly metabolised in the liver and incorporated into phospholipids in cellular membranes via the formation of phosphoryl ethanolamine and cytidinediphosphate ethanolamine (HSE 2016, SCOEL 1996). Excess MEA is converted via acetaldehyde to carbon dioxide and exhaled. In a study of dermal uptake in mice (Klain et al. 1985), MEA was widely distributed and extensively metabolised. Following inter-peritoneal injection in rats, the highest concentrations were reported in the fatty tissues of the spleen, kidneys and small intestine (Taylor and Richardson 1967).Urea, glycine, serine, choline, and uric acid were the major urinary metabolites in mice (Klain et al. 1985).

#### **Short- and Long-term Exposures**

The acute toxicity of MEA is low (SCOEL 1996), but it is a respiratory, ocular, and skin irritant (HSE 2016, TCEQ 2015). No deaths or abnormal clinical signs after 14-days were reported in Sprague-Dawley rats exposed to 1,300 mg/m3 for 6 hours (a proprietary study conducted in 1988). [[1]](#footnote-1) Necropsy findings were also reported to be ‘unremarkable’. In a sub-acute study, Wistar rats exposed to a respirable MEA aerosol at >50 mg/m3 for 6 hours per day, 5 days per week showed signs of respiratory irritation including submucosal inflammation and squamous metaplasia in the larynx and trachea.[[2]](#footnote-2)

Repeated continuous exposure at levels above 66 ppm (168 mg/m3) caused pathological lesions to the lung, liver, kidneys, spleen and testes in dogs, guinea pigs, and rats exposed for up to 90 days (Weeks et al., 1960).[[3]](#footnote-3) Dogs exposed at 66 mg/m3 showed immediate signs of restlessness and discomfort, indicated by nose-pawing, muzzle-licking, and shallow-rapid respiration. Exposure of rats, dogs and guinea pigs to MEA vapour was also reported to produce skin irritation at levels as low as 5 ppm (13 mg/m3), although SCOEL (1996) suggested that this may have been potentiated by direct skin contact with liquid that had condensed on the surface of the inhalation chamber. Localised respiratory inflammation was also observed at concentrations >50 mg/m3 in Wistar rats exposed for 6 hours per day, 5 days per week, for 4 weeks (proprietary study, see Pivotal Studies).

Respiratory sensitisation resulting in occupational asthma has been identified as a concern by CNESST (2019), but this opinion has been disputed (HSE 2001 and 2016, SCOEL 1996). Although several case reports (Gelfand 1963, Makela et al. 2011, Sallie et al. 1994, Savonius et al. 1994) have identified symptoms of respiratory sensitisation, there are difficulties in interpretation due to concomitant exposures, uncertainties in the concentration and duration of exposure, and other factors such as the sensitivity of those studied to multiple allergies. HSE (2016) noted that symptoms of occupational asthma had been identified in only a limited number of case reports despite the widespread use of MEA. In a mechanistic study by Kamijo et al. (2009) significant bronchoconstriction was observed in guinea pigs, but there was no evidence of respiratory sensitisation (HSE 2016). The authors suggested that the mechanism for bronchoconstriction possibly involved agnostic effects at the histamine H1 and muscarinic receptors.

Evidence for neurobehavioral effects have been reported. Repeated inhalation exposure at levels above 66 ppm (168 mg/m3) caused neurobehavioral changes in dogs, guinea pigs, and rats exposed continuously to MEA vapour for up to 90 days (Weeks et al., 1960). Rats exposed for 2-3 weeks to 5 ppm (13 mg/m3) exhibited lethargy (Weeks et al. 1960).

Evidence for reproductive toxicity has also been reported (Weeks et al. 1960, Mankes 1986), but SCOEL (1996) concluded that this occurred at exposure levels much higher than those that induced either irritation or neurobehavioral effects.

#### **Genotoxicity and Carcinogenicity**

*In vitro* genotoxicity was investigated in three bacterial reverse mutation assays, a chromosome aberration assay in rat hepatocytes and two mammalian cell gene mutation assays (mouse lymphoma [L5178Y] and Chinese hamster lung fibroblasts [V79]). Negative results were reported in all studies (HSE 2016). Negative results were also obtained from an *in vivo* mouse micronucleus test where clear signs of substance related toxicity were observed at the highest dose. HSE (2016) concluded that based on the tests performed, the results for MEA were consistently negative and that they gave no cause for additional concerns. SCOEL (1996) also reported that MEA was not mutagenic in bacteria and did not induce cell transformation.

No specific carcinogenicity studies have been reported (HSE 2016, SCOEL 1996). HSE (2016) noted that hyperplasia and metaplasia were observed in the respiratory tract in the 28-day proprietary study with Wistar rats (see Pivotal Studies). However, they concluded that MEA is a corrosive substance and that the relevance of these respiratory tract lesions to human carcinogenicity was questionable.

#### **Pivotal Studies**

In a sub-acute study submitted as evidence in support of an application under REACH (HSE 2016), Wistar rats were exposed to a respirable MEA aerosol at 10 mg/m3, 50 mg/m3, or 150 mg/m3 for 6 hours per day, 5 days per week, for 4 weeks.2 Each concentration group consisted of 10 rats (5 of each sex). Animals were monitored for mortality, clinical signs of toxicity, bodyweight, food consumption, ophthalmological effects, haematological and clinical chemical effects, and were subject to necropsy at the end of the study including gross pathology and histological investigation. No systemic effects were observed at any concentration level. No histopathological effects were seen in any other organ outside the respiratory tract. Exposure at 150 mg/m3 resulted in submucosal inflammation (levels I, II) in males and females, degeneration of submucosal glands (level I) in males and females, focal epithelial necrosis (level I) in males and females, focal squamous metaplasia, (level I) in males and females; (level II) in one male and two females and focal epithelial hyperplasia (level II) in males and females were observed in the larynx. In the trachea, focal squamous metaplasia (carina) accompanied by inflammation in males was observed. At 50 mg/m³ submucosal inflammation (level I and II) in males and females and squamous metaplasia (level I and II) in few males and females in the larynx was reported. No treatment-related weight changes, gross lesions or microscopic findings at the low concentration (10 mg/m3). HSE (2016) concluded that the NOAEC for localised and systemic effects were 10 mg/m3 and 150 mg/m3, respectively.

In a sub-chronic study by Weeks et al. (1960), male adult beagles (n=3 per exposure group), six-week old male guinea pigs (n=22 or 30 per group), and eight-week old female rats (n=45 per group) were exposed continuously exposed to MEA at concentrations of 12 – 26 ppm (30.5 – 66.0 mg/m3), or 66 – 102 ppm (167.6 – 259.1 mg/m3) for between 24 and 90 days. Additionally, 4-6 week old male and female rats (n=20) and male beagles (n=3) were exposed to 5 – 6 ppm (12.7 – 15.2 mg/m3) for 40 and 60 days, respectively.

Dogs tolerated a much higher concentration of MEA than rodents, with two dogs surviving 30-days exposure at the highest doses (167.6 – 259.1 mg/m3). At their respective highest dose, 83% of the rats and 75% of the guinea pigs died after 28- and 24-days exposure, respectively. The two surviving dogs developed lung irritation (i.e., moist rales) by the middle of the second week, which was associated with a low grade fever that ran a course of about 2 weeks. Depressed, lethargic, and apathetic states were noted in all animals that survived the high dose. Other common effects like skin lesions on ground contact points (feet, nose, lips, and chin) and skin points of tension (around extensor surface of larger joints) showed dark eschars (i.e., dry scabs that form on burned skin) which covered ulcerated skin beneath. These skin-related effects may be associated with the animals constantly in contact with MEA condensate as it accumulated on the walls and floors of the exposure chambers throughout the experiments.

All animals survived their respective intermediate concentrations (30.5 – 66.0 mg/m3) of MEA vapour for 90 days. Signs and symptoms were similar to those seen at the higher concentrations, but not so severe. Dogs exposed to 66.0 mg/m3 showed “immediate” signs of restlessness and discomfort, indicated by nose-pawing, muzzle-licking, and shallow-rapid respiration (whilst the specific duration is not stated, as irritation is primarily concentration-dependent, it was assumed the “immediate” irritant effects reported would also occur at a 1-hour duration). Throughout the experiment these dogs were more irritable than controls, and after a few days of exposure were less alert and bordered variably on lethargy. Slight tremors of rear leg muscles were also noted. Also, skin at floor contact points on the chest and scrotum of the dogs became irritated, which was relieved by ointment.

Dogs exposed to 30.5 mg/m3 for 90 days did not show immediate behavioural changes. No significant weight changes occurred nor did physical examinations reveal any changes. However, after several days their skin became irritated and soothing ointment was applied, which relieved the condition and the skin showed no further signs of irritation. Concurrently, lethargy or depression appeared and lasted about three weeks before their behaviour returned to normal. Rodents exposed to 30.5 – 38.1 mg/m3 became less active than the controls after about 3 days, and showed definite lethargy after about 10 days, which lasted throughout the balance of the exposure. In addition to hair loss, rodents showed an approximate 10% reduction in weight gain and approximately a 40% increase in water consumption.

For the low exposure group, young (4-5 weeks old) male and female rats and mature beagles were exposed to 12.7 – 15.2 mg/m3 for 40 days and 60 days, respectively. All animals survived exposure to these low concentrations. Neurobehavioral changes in animals were noted after 2-3 weeks of continuous exposure at these concentrations. In dogs, a slight decrease in alertness and activity was noted. 2 of the three exposed dogs also showed slight weight loss concurrently. No changes from normal were observed in pulse, temperature, and heart and lung sounds. Skin irritation and hair loss occurred on chest-floor contact areas, and the scrotum became bare and spotted with small scattered black eschars. All rats exposed to 12.7 mg/m3 showed pelt discoloration after 12 days and transitory hair loss on the head and back after 3 weeks, which was more pronounced in the females. Additionally, some slowness in movement developed in rats after 3 weeks, which lasted throughout the 40-day exposure duration.

Based on the results of this study, 30.5 mg/m3 was selected by TCEQ (2015) as the acute LOAEC for nasal irritation symptoms (e.g., nose-pawing, shallow breathing) in dogs. Neurobehavioral changes seen in rats and dogs at 12.7 mg/m3 were selected by TCEQ (2015) and HSE (2016) for the chronic LOAEC.

### Short-term Exposure

HSE (2016) and TCEQ (2015) have proposed HBGVs for MEA.

#### **Health and Safety Executive**

HSE (2016) proposed a DNEL of 3.8 mg/m3 to protect the general public from local and systemic effects from acute exposure. It was based on the 15-minute STEL of 7.6 mg/m3, which had been recommended by SCOEL (1996) to prevent worker exposure to irritating levels. In the study by Weeks et al. (1960), exposure of rats, guinea pigs, and dogs to MEA vapour had produced skin irritation at levels as low as 12.7 mg/m3. HSE (2016) applied a further UF of two to account for wider sensitivity in the general population.

#### **Texas Commission on Environmental Quality**

TCEQ (2015) proposed an acute Air Monitoring Comparison Value (AMCV) of 0.32 mg/m3. It was based on a NOAEC of 30.5 mg/m3 for behavioural signs of nasal irritation (nose-pawing, shallow breathing) in dogs subject to continuous exposure for up to 90 days (Weeks et al. 1960). A UF of 90 was applied (a factor of 3 for interspecies variation, a factor of 10 for intra-species variation, and a further factor of 3 for deficiencies in the database for acute toxicity). No adjustment was applied to the use of a sub-chronic study because irritation was considered a concentration-based effect.

### Long-term Exposure

HSE (2016), TCEQ (2015), and the industry REACH dossier have proposed HBGVs.

#### **Health and Safety Executive**

HSE (2016) derived a DNEL of 0.5 mg/m3 to protect the general public from systemic effects from long-term exposure. It was based on the OEL of 2.5 mg/m3 as an 8-hour TWA derived by SCOEL (1996), which itself used the LOAEC of 12.7 mg/m3 for signs of lethargy and sluggish movement seen in rodents (Weeks et al. 1960) and a UF of 5 for interspecies variation. HSE (2016) corrected the OEL to continuous exposure (8/24) and divided it by an additional UF of 2 for wider sensitivity in the general population.

#### **REACH Chemical Dossier**

The industry REACH dossier for MEA on the ECHA dissemination portal derived a DNEL of 2 mg/m3 to protect the general public from localised effects from long-term exposure. [[4]](#footnote-4) It was based on a NOAEL of 10 mg/m3 from a proprietary sub-acute study in Wistar rats for inflammation and lesions in the respiratory tract (see Pivotal Studies). Concentration was considered more important than exposure duration for an irritant effect and therefore no correction was applied for intermittent exposure. A UF of 5 was applied (a factor of 1 for interspecies variation and a factor of 5 for intra-species variation).

#### **Texas Commission on Environmental Quality (TCEQ)**

TCEQ (2015) proposed a chronic AMCV of 0.023 mg/m3, which was based on a LOAEC of 12.7 mg/m3 for signs of lethargy and sluggish movement observed in rodents (rats and guinea pigs) exposed to MEA vapour for up to 90 days (Weeks et al. 1960). A UF of 540 was applied (a factor of 3 for extrapolation from a LOAEC to NOAEC, a factor of 3 for interspecies variation, a factor of 10 for intra-species variation, a factor of 2 for the sub-chronic to chronic exposure duration, and a factor of 3 for deficiencies in the database for chronic toxicity).

### Summary

Several authoritative organisations have proposed HBGVs for MEA, although the overall toxicological database is small.

Short-term exposure guidelines have been proposed by HSE (2016) and TCEQ (2015) based on localised irritation observed in rodents (rats and guinea pigs) and dogs in a repeat dose inhalation study (Weeks et al. 1960). Although TCEQ (2015) used a higher LOAEC of 30.5 mg/m3 as the POD, they also applied a larger UF, which lead to a lower guideline.

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| **Summary of Health-based Guidance Values for Short-term Exposures** |
| **Guideline** | **Value (mg/m3)** | **Duration** | **Critical effect(s)** | **Pivotal reference(s)** |
| Current EAL | None | - | - | - |
| AMCV | 0.32 | 0.5 – 1-hour | Irritation | Weeks et al. 1960 |
| DNEL (HSE 2016) | 3.2 | 15-mins | Irritation | Weeks et al. 1960 |

Long-term chronic exposure guidelines were proposed by HSE (2016), TCEQ (2015), and the industry REACH dossier. HSE (2016) and TCEQ (2015) used the same endpoint of neurobehavioral effects seen in rodents and dogs (Weeks et al. 1960), whilst the industry REACH dossier used respiratory irritation observed in a sub-acute rodent study (see Pivotal Studies). The POD were similar (10 or 12.7 mg/m3) and the wide difference in health-based guidance values is explained by the choice of UF (5, 10, and 540).

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| **Summary of Health-based Guidance Values for Long-term Exposures** |
| **Guideline** | **Value (mg/m3)** | **Duration** | **Critical effect(s)** | **Pivotal reference(s)** |
| Current EAL | None | - | - | - |
| AMCV | 0.023 | Life-time | Neurobehavioral | Weeks et al. 1960 |
| DNEL (HSE 2016) | 0.5 | Life-time | Neurobehavioral | Weeks et al. 1960 |
| DNEL (REACH dossier) | 2 | Life-time | Irritation | Proprietary Study 2010 |

### Recommendations

#### **Short-term EAL**

The critical health effect from short-term inhalation exposure to MEA vapour is considered to be localised respiratory irritation. The pivotal study for the derivation of a short-term EAL is the sub-acute duration rodent study submitted as evidence in support of an application under REACH (HSE 2016). In this study, Wistar rats were exposed to a respirable aerosol at 10 mg/m3, 50 mg/m3, or 150 mg/m3 for 6-hours per day, 5 days per week, for 4 weeks. The POD is considered to be the NOAEC of 10 mg/m3, which was identified for localised irritation of the respiratory tract (HSE 2016). No correction for continuous exposure is applied to the POD because irritation is considered a concentration-dependent effect. The short-term EAL of 0.4 mg/m3 is obtained by dividing the POD from a relevant sub-acute animal study by a UF of 25 (a factor of 2.5 for interspecies variation and a factor of 10 for intra-species variation). This is consistent with the approach to the derivation of an acute DNEL for respiratory irritation under REACH.

#### **Long-term EAL**

The critical health effects from long-term inhalation exposure are considered to be respiratory irritation and neurobehavioral toxicity. In accordance with the guidance for the derivation of EALs, the DNEL proposed by HSE (2016) would be recommended as the long-term EAL because it was proposed by a UK authoritative body. However, it is derived from the OEL proposed by SCOEL (1996). Most notably, HSE (2016) corrected for continuous exposure from the OEL (8 hours to 24 hours) despite the observation that the underlying study by Weeks et al. (1960), on which the OEL was based, used a regime of continuous and not intermittent exposure. The high UF adopted by TCEQ (2015) in the derivation of the chronic AMCV is considered a little over-cautious. Therefore the pivotal study for the derivation of a long-term EAL is considered to be the same sub-acute rodent study used for the short-term EAL. The POD is considered to be the NOAEC of 10 mg/m3, which was identified for localised irritation of the respiratory tract (HSE 2016). The long-term EAL of 0.1 mg/m3 is obtained by dividing the POD by a UF of 100 (a factor of 10 for interspecies variation and a factor of 10 for intra-species variation). No factor for sub-acute to chronic duration is required because irritation is considered a concentration-based effect.

### Abbreviations and Definitions

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| AMCV | Air Monitoring Comparison Values are established in the State of Texas to evaluate the potential effects as a result of exposure to chemicals in air. They are not considered ambient air standards. Exceedances do not necessarily indicate a problem, but triggers a more in-depth review. |
| DNEL | Derived No-Effect Level is defined as the level of exposure to a substance above which humans should not be exposed. DNEL apply to health effects with a threshold. |
| EAL | Environmental Assessment Level |
| ECHA | European Chemicals Agency |
| HBGV | Health-Based Guidance Value |
| HSE | Health and Safety Executive |
| LOAEC | Lowest Observable Adverse Effect Concentration |
| NOAEC | No Observed Adverse Effect Concentration |
| OEL | Occupational Exposure Limit are broadly defined as a measurable concentration of a substance in air that represents a point of reference for the development of workplace strategies to protect workers from health risks associated with inhalation of chemical substances. |
| POD | Point of Departure |
| REACH | Registration, Evaluation, Authorisation and Restriction of Chemicals is a European Union regulation that addresses the production and use of chemical substances and their potential impact on human health and the environment. |
| STEL | Short-term Exposure Limit (usually 15 minutes) for use in the workplace |
| UF | Uncertainty Factor |

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1. : <https://echa.europa.eu/registration-dossier/-/registered-dossier/15808/7/1> [↑](#footnote-ref-1)
2. : <https://echa.europa.eu/registration-dossier/-/registered-dossier/15808/7/1> [↑](#footnote-ref-2)
3. : 1 ppm = 2.54 mg/m3 (SCOEL 1996). [↑](#footnote-ref-3)
4. : <https://echa.europa.eu/registration-dossier/-/registered-dossier/15808/7/1> [↑](#footnote-ref-4)