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Substance Prioritisation for the Development of EU Acute Exposure Toxicity Thresholds: Risk-Informed Decision Making

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Abstract

The aim of the EU ACUTEX project is to develop a methodology for establishing European Acute Exposure Threshold Levels (EU AETLs) for toxic substances in relation to harm to people by inhalation. Their development is initially in the context of the EU ` Seveso II' Directive through which the risks of major accidents from chemical sites are regulated. This paper describes the prioritisation of 21 substances for AETL case studies based on an EU stakeholder consultation exercise. It also outlines progress on the subsequent development of a prioritisation methodology to inform initial substance selection for a possible further AETLs programme.

1. Introduction: The EU ACUTEX Project

The process industry in the EU is large and innovative. For example, the chemicals sub-sector is responsible for over a third of world chemicals production. Yet, on average there are some 30 major accidents every year in the EU[1] and accidents worldwide have further demonstrated the potential for disaster. Probably the worst catastrophe in the history of the chemical industry was at Bhopal, India, in 1984. A dense cloud of toxic gas drifted from the site over the surrounding shanty town killing over 2,000 people and permanently disabling over quarter of a million more.

In the EU, the risks of major accidents from chemical sites are regulated through the `Seveso II' Directive for the Control of Major Accident Hazards Involving Dangerous Substances [2]. This includes both accident prevention and mitigation.

[1] According to the information in the EU `MARS' database which gives [1] 417 major accidents over 14 years for notifiable major accidents under the Seveso II Directive and the earlier Seveso I Directive.

Here, accident mitigation refers to limiting the consequences of accidents through both land-use planning and emergency planning including the provision of information to the public near sites. For sites with the potential to release toxic substances, decisions on accident prevention and mitigation are informed by estimations of dispersion distances for various foreseeable events based on the toxicology of the material involved and the extent and severity of likely harm.

The aim of the EU ACUTEX project is to develop a methodology for establishing European Acute Exposure Threshold Levels (EU AETLs) for toxic substances for use, initially, in this context. It is intended that the ACUTEX project will provide a broadly accepted, scientifically sound methodology for developing EU acute exposure thresholds which can be adapted, where appropriate, to the various national situations in land-use planning or emergency planning, and which will complement existing thresholds developed by Member States (or industry or other organisations). Additionally, it is intended that through collaboration between toxicologists in the EU, and promotion of sharing data and expertise, the overall cost of producing these thresholds will be reduced. AETLs will not have an EU regulatory status: whether and how AETLs might be used in individual Member States is the responsibility of policy makers at Member State level.

The AETLs for a substance will define the exposure conditions in terms of airborne concentration and exposure time that will produce a series of specified levels of harm to people. These levels of harm have not yet been finalised, but they are likely to range from transient discomfort at the lower end of the scale to severe long-lasting adverse health effects and, at the upper end of the scale, life threatening effects or death. Additionally, it is intended that the AETL methodology will complement the toxicological principles established in the US Acute Exposure Guideline Levels (AEGLs) programme [3].

As part of the methodology development, AETLs will be produced for 21 substances as case studies. In line with the ACUTEX project's aims, the scope of substances for selection as case studies is those substances covered by the Seveso II Directive in terms of their toxic properties[2]. A wider scope is likely to be given consideration for any further programme of AETLs.

One possible outcome following the ACUTEX project is a further EU programme of AETLs development. The decision on whether AETLs are most suitable to meet EU needs will be informed by the outcome of ACUTEX.

The ACUTEX project started on 1st December 2002 and has a planned duration of 3 years. It is funded under the EU's Fifth Framework Programme of Research. The project has 9 partner organisations in which government, researchers and industry are represented and is lead by the French Institut National de l'Environment et de Risques (INERIS). The project is being monitored by a Critical Review Panel (CRP) comprising experts from major EU stakeholder groups including emergency planners, industry, Competent Authorities (the EU Member State enforcing authorities for the Seveso II Directive), toxicologists, and risk-related decision makers. The CRP is chaired by the European Commission's Major Accident Hazards Bureau (MAHB).

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[2] The scope is the Named Carcinogens and substances classified as Toxic or Very Toxic including any Named Substances as specified in the Seveso II Directive.

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2 Substance Prioritisation for AETLs Development

Substance prioritisation is important to various aspects of risk regulation and is widely carried out. A review of priority setting systems was included in the 1986 OECD expert groups' publication [4] as part of their remit for the `rational, pragmatic and cost-effective' selection of existing chemicals, while more recently an international workshop produced a framework within the context of chemical risk assessment and management [5].

As part of the ACUTEX project, the Health and Safety laboratory (HSL) worked with the Health and Safety Executive (HSE) to develop the prioritisation methodology which informed the selection by decision makers drawn from the ACUTEX project of 21 preliminary priority substances for AETL case studies. The methodology is described below and full details are given in [6]. Additionally, we are now developing a further prioritisation methodology to inform the initial selection of substances for which AETLs would be developed under any further AETLs programme: progress is outlined below. Our role as analysts is to work with and provide technical support to the decision makers. At each stage of the work, the views of the ACUTEX decision makers and the major EU stakeholders are being sought in order to ensure that their priorities are fully addressed. It is intended that the methodologies should facilitate both the decision making process and its transparency by providing a common, agreed framework. This is within the context of the principles in the European Commission White Paper on Risk Governance [7] including the need for openness and the fair treatment of all Member States. A discussion of risk analysis within regulatory decision-making, based on a workshop held at the European Commission's Joint Research Centre, is given in [8].

2.1 Factors of Importance to Stakeholders

The first stage of development of both substance prioritisation methodologies was to identify 'factors of importance' to stakeholders for prioritisation. A stakeholder consultation exercise was initiated and coordinated by MAHB, acting as chair of the CRP, to elicit the views of major European stakeholders represented on the CRP and of EU Competent Authorities and EU Candidate States. Stakeholder views included those of the European Chemical Industry Council (CEFIC) following a workshop they held on ACUTEX.

The exercise confirmed that the longer term issue for prioritisation is: `What is the most cost-effective choice of substances for AETL development in order to reduce off-site risk to the public from Seveso II sites, given that it is intended that AETLs can be used within Member States, if appropriate, to inform decisions on emergency planning or land-use planning?'. However, for selection of the 21 case studies it is paramount that the ACUTEX research needs are met.

2.2 Prioritisation of 21 Case Study Substances

All EU Member State Competent Authorities and Candidate States were invited by MAHB to propose an initial list of substances of interest for AETLs development. These substances formed the basis for selection of the 21 case studies. Ten Member

States replied. The degree of consensus in the replies was noteworthy. For example, approximately 30% of the substances which were within the scope of the ACUTEX case studies were proposed by more than one Competent Authority.

The prioritisation methodology is in the form of: 12 selection criteria with priorities as shown in table 1; and a spreadsheet giving information such as toxicity and physicochemical properties relevant to these criteria for each substance. The criteria do not aim to select exclusively the highest risk substances in the EU. For example, an essential criterion is to test the AETL methodology against a range of substances with diverse toxicological properties classified according to 15 `key adverse health effects' ranging from effects on fertility to eye irritation. A specific consideration was the need to include a `Named Carcinogen' from the Seveso II Directive. These are substances that may have a carcinogenic effect after a single exposure. This was the only criterion that could not be met from the substances proposed by the Competent Authorities. In discussion with CRP and ACUTEX experts, hydrazine was selected as it has appropriate data and is in relatively widespread use in the EU.

Table 2 gives the preliminary list of 21 case study substances: it may be reviewed according to the emerging findings of the AETLs methodology development. For example, four substances were included because they were proposed by 6 of the 10 Competent Authorities: hydrogen fluoride which is used in the production of lead-free petrol; chlorine which is produced in bulk for drinking-water treatment; hydrogen chloride which can be released following the spillage of various water-reactive substances; and hydrogen sulphide which is widely used as a reagent in chemicals production and which can also potentially be released as a reaction product. Aniline is an example of a substance selected because it leads to one of the 15 key adverse health effects: it is a widely used starting material for the production of synthetic dyes, and can reduce the ability of the blood to carry oxygen due to the formation of methaemoglobin.

2.3 EU Prioritisation Methodology for Possible Further AETLS

It is envisaged that the EU priority substance list for any further AETLS programme will be selected by decision makers based on priority substance lists proposed by Competent Authorities. Priorities at Competent Authority level might be informed by, for example, the toxicity and physicochemical properties of substances (their `inherent properties'), numbers of sites, and the population that could potentially be exposed[3]. For the EU prioritisation methodology, issues to be established at this stage include an indication of the total number of substances of concern, and the degree of consensus among priority substances for the various Competent Authorities. Both of these factors influence the information that Member States will need to supply, and whether the prioritisation methodology will require more than one stage. For example, it may be appropriate to collate information[4] on numbers of

[3] For a discussion of the analysis of risks from chemical sites see, for example, [9].
[4] The EU `SPIRS' database (see [1]) holds information on numbers of sites for the Named Substances and Generic Categories of Substances as defined in the Seveso II Directive. However, because SPIRS is based on the requirements of the Seveso II Directive, the information is not broken down by substance within the Generic Categories.

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Category		P	Description
A) In ACUTEX Case Studies Scope		1	Select substances in scope
B) Meet ACUTEX Research Needs	Bi) Meet Needs of Toxicologists for Development of AETLs Methodology	1	Select at least one `Seveso II' Named Carcinogen
		1	Select one (but not more than one) substance with poor toxicological database and no AEGL
		1	Select at least 3 Substances with poor toxicological database for which an AEGL exists
		1	Select at least one substance with each of 15 Key Adverse Health Effects
		3	Avoid over-representation of upper-respiratory tract irritants
		3	Select 1 substance only from groups with very close structural and relationship and toxicological properties
	Bii) Allow Comparison with US AEGLs	1	Select at least 5 substances with an AEGL.
C) Maximise Usefulness of 21 AETLs Developed as Case Studies for Use as Appropriate in EU Member States	Ci) High Risk/ Concern across EU	2	Give priority to substances nominated by more than one Member State
		4	Give priority to substances with greatest potential to cause adverse health effects, based on physicochemical and toxicological hazardous properties (optional criterion not needed in practice)
	Cii) Representative of Seveso II Chemical Plant	2	Select at least one solid, liquid and gas
		2	Select substances stored as liquids to cover a range of vapour pressure and toxicity

Table 1: Criteria For Case Study Prioritisation with Category and Priority (P) where 1= Essential, 2=Highly Desirable, 3= Desirable and 4 = Optional.

Acrylonitrile	Allylamine	Ammonia
Aniline	Carbon disulphide	Chlorine
Dichlorophenyl isocyanate	Ethylene oxide	Hydrazine
Hydrogen chloride	Hydrogen fluoride	Hydrogen sulphide
Methanol	Nitrogen dioxide	Oxybenzene (phenol)
Phorate	Phosgene	Phosphorous trichloride
Propionitrile	Sulphur dioxide	Toluene diisocyanate

Table 2: The Preliminary 21 AETL Case Study Substances: May be Reviewed According to Emerging Findings of AETLs Methodology Development

sites for those substances that are not of priority to several Member States. It is important that information requirements made on Member States are as simple as is compatible with transparent and robust decisions so that the costs of prioritisation are minimised.

We are carrying out a validation exercise with two (or possibly three) Competent Authorities. Since Member States' final priorities for AETLs will depend on the outcome of ACUTEX, this exercise is solely to inform the development of the prioritisation methodology. Results are now available from HSE for the UK. Approximately 1,100 UK chemical sites are regulated under the Seveso II Directive of which about 40% are regulated in terms of the potential for release of toxic substances. Subject to UK stakeholder consultation, there are 156 priority substances of which 31 are judged to be high priority. About 50% of these high priority substances (17 substances) have already been proposed by another Member State including 14 substances that have already been included in the 21 case study substances. This gives a preliminary indication that the degree of consensus among Member States' priority substances may support an initial high priority EU list based on substances that are nominated as high priority by several Member States, together with consideration of these substances' potential to cause adverse health effects based on their inherent properties.

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