Exposure scenarios and exposure modelling for biocidal products

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Summary

Under current European and national legislation, biocidal products must be registered based on a risk assessment with respect to humans, animals and the environment. Especially human exposure assessment shows many white spots in knowledge, which make it hardly possible for many biocidal application scenario's to assess health risks in a proper way. A European-funded project has tackled this issue and ways are described to deal with the problem in an appropriate fashion. The approach is accepted by the European Commission for the Biocidal Product Directive as a TnG (Technical notes for Guidance [Van Hemmen et al, 2002b]). In the present paper only worker exposure will be considered.

Samenvatting

De recente Europese biociden richtlijn, die in de wet- en regelgeving van de lidstaten reeds is (bijv. in Nederland) en deels nog wordt geïmplementeerd vereist registratie van alle biocide producten alvorens ze op de Europese markt worden gebracht. Onderdeel hiervan is een beoordeling van de risico's van het gebruik van die producten voor mens, dier en milieu. Met name voor de beoordeling van de risico's voor mensen bestaan er zeer veel hiaten in onze kennis van blootstellingsprofielen zodat een risicobeoordeling nauwelijks mogelijk is. Voor dit doel is een Europees gefinancierd project (voor Nederland gesteund door het Ministerie van SZW en VWS) gestart om te komen tot bruikbare benaderingen voor die blootstellingen. Het rapport is overgenomen door de Europese Commissie als een TnG (Technical notes for Guidance [Van Hemmen et al, 2002b]), te hanteren bij de implementatie van de Richtlijn. In het onderhavige artikel wordt alleen aandacht besteed aan de blootstelling van de werkers.

Introduction

The Biocidal Product Directive 98/8/EC requires registration of biocidal products on the basis of a risk assessment of their uses. The Directive is currently being implemented in member state laws and initial studies have been carried out to investigate the approaches as laid down in the various regulations. This pilot programme is finished early 2001. There are 23 different biocidal product types, in four major groups:

- disinfectants and general biocidal products
- preservatives
- pest control products
- other biocidal products.

A major shortcoming in our present knowledge is the assessment of human exposure. This was also shown in the indicated pilot programme.
To fill this knowledge gap, a project proposal by 7 Institutes/organisations (amongst which TNO and RIVM) from 6 European member states, together with two representatives from CEFIC, the producing and formulating industry in Europe, was accepted by DG Environment (B4-3040/2000/291079/MAR/E2). The project has delivered its final report mid 2002, and it was positively discussed at member state level and community level (by experts at a Technical Meeting and by policy-makers at a Competent Authorities meeting).

The aims of this project were:
- to develop relevant exposure scenarios of humans to biocidal products
- to develop operational predictive model(s) and guidance on how to use these for the purpose of registration of the various biocidal active substances in the many different use and exposure scenarios identified.

Methods

The project focuses on exposures to workers and consumers. In the present paper only results with respect to worker exposure will be discussed.
To assess exposure to biocidal products for risk assessment purposes, one needs to know the *'patterns of use'* for the product:
- the product (physical state, package form, etc.) and its purpose
- where, how and by whom it is used
- expected control measures
- tasks, frequencies and durations
  - for mixing/loading
  - for application
  - for post-application activities (secondary exposures)
- who else may be exposed (bystanders).

Occupational exposure data have been requested from industry (sectors), governmental agencies, and academia from

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North America and Europe. All these publications have been quality-assessed based on pre-developed criteria, regarding aim (design), documentation and analytical-chemical quality aspects. From the study reports that were considered adequate, data are subtracted and compiled in series of databases. This approach is very similar to the one taken for the EUROPOEM database [Van Hemmen, 2001b; EUROPOEM, 1996]. For use of the databases two different approaches are taken. These are both based on the assumption that for most biocidal uses (applications), the exposure is task-based and not dependent on specific chemical properties of the biocide. This means that extrapolation from one study to another is possible when the exposure data have a suitable format and the exposure scenario (series of tasks, preferably one task) is similar. This may not be true for all tasks, so a careful judgement of the tasks involved is required for this purpose.

Results

First approach

For some tasks the database of exposure provides an adequate series of study results, meaning that for that task a predictive exposure model is developed. The models (databases) that could be developed are presented in the report of the current project. Using all appropriate data, a matrix is developed with two axes: one for width of distribution and one for central tendency of distribution. All available study data are entered in the matrix at the right cell(s), as shown in Table 1. These cells can -in time- be filled with additional (new) exposure data.

The matrix has four typical central tendency values (GM), varying from 4 mg/min (low), 20 mg/min (medium), to 100 mg/min (high) and 500 mg/min (top), expressed as amount of in-use product. The other axis involves the width of the distribution and its GSD varies from 2.45 (narrow), via 3.36 (intermediate) to 6.04 (wide). From this description it is clear that log-normal distributions have been assumed for these exposures, and the typical cell values have been chosen to accommodate the current experimental study results.

The databases are described with respect to the involved tasks and have been evaluated for relevant levels of exposure using 75-percentile values for typical exposure levels and 95-percentiles for 'reasonable worst case exposures'. These values are used for chronic health effects, whereas the 95-percentiles are proposed for use in case of acute health effects. 95-Percentiles may also be used to ascertain possible levels of exposure in case of foreseeable misuse. Data are available for hand and body exposure , and for inhalation exposure.

If the task under consideration is not available in the matrix then the exposure assessor should present arguments for specific choices for an exposure cell in the matrix. If there is some doubt, a higher width and higher typical value should be chosen. If no arguments at all can be presented for specific choices, the assessor is forced to choose for the cell with the largest width and highest typical value. This forces industry (registrants) to produce data for that specific task or set of tasks (use scenario).

Approaches are being prepared for choices between separate (suitable) models, and several examples have been worked out to indicate the use of these data.

Second approach

Bayesian statistics are used to develop an exposure assessment for tasks that have no specific exposure model, but do have assessable (dis)similarities with all the other sets of data in the matrix. In this approach, called BEAT (Bayesian Exposure Assessment Toolkit), all databases (for the time being only for body exposure) have been computerised and are transformed into distributions with discrete GMs (geometric means) and GSDs (geometric standard deviations).

For a new task (or scenario) that can be described in terms of similarity or dissimilarity a set of questions must be answered and entered into the model. Using Baye's theorem, the (dis)similarities are calculated for all the databases in the model, leading to a new distribution which is then fitted to

Table 1. A predictive exposure model

		Central tendency value			
		low	**medium**	**high**	**top**
Width of distribution	**narrow**	* timber pre-treatment (solvent) * cda spraying *trigger spray	* anti-foul mixing and loading * flea dusting * brushing overhead	* spraying overhead * aerosol space spray	
	intermediate		* low pressure spray * timber pre-treatment (aqueous) * anti-fouling brushing	* anti-fouling spray	* sheep dipping
	wide	* fence brushing		* medium pressure spraying * dipping	

the cells of the above-mentioned matrix (Table 1), since this is used to model the output in terms of maximum likelihood that the distribution fits into the various cells.
The so-called rule base for assessing the degree of similarity between tasks (scenarios) determines of course the output from the model. The rule base is determined on the basis of expert knowledge from field experience.
Its validity has been checked internally, by taking a study out and entering it again using the rule base. External validity can be determined using a new task (scenario) and assessing it on the basis of the rule base and concomitant comparison with actual field data to be collected.
In principle there is no problem to add a rule base for inhalation exposure data and hand exposure data. The databases for these exposures are already in the computerised approach.
The BEAT model in its current incomplete version is available from the project team on a CD-ROM. The mathematical approach used is currently being described [Warren, 2003].

Secondary exposure
There are currently hardly any data for post-application exposure. Some 'reference scenarios' have been developed that might help in estimating the most relevant exposures. These scenarios can only be handled for the exposure viewpoint with conservative assumptions and will thus require further exposure studies which will then help to obtain more realistic assumptions and possibly suitable databases.

'Patterns of use'
The required 'patterns of use' have been described for all known (to the project team) uses of each product type and post-application scenarios in some detail. There is, however, a strong need to extend this with data obtained form industry. In the Netherlands this is tackled by carrying out survey's (TNO and SZW) to obtain the required information [Van der Jagt, unpublished].

Discussion and conclusion

The Bayesian approach for modelling, which combines objective and subjective data, is being considered and will be subject of validation exercises. The rule base currently covers only body exposure.

Exposure scenarios ("patterns of use") are described for all 23 biocidal product types.
Guidance is written -with many worked out examples- to enable authorities and registrants to do exposure assessments in a harmonised way, throughout European member states, with quite a bit of specific expertise still required for use.

Development of the BEAT model will continue for quite some time. The current idea is first to validate/benchmark the current system with only body exposures, using a large representative field study, and secondly extend this to hand exposure and inhalation exposure, which require different rule bases. Thirdly, it is the intention to also include the exposure data from other European exposure databases under development, such as RISKOFDERM [Van Hemmen et al, 2001a, 2002a] and EUROPOEM [Van Hemmen, 2001b].

It is hoped by the authors of the project report that the report will be considered a 'living document' that will be updated and adapted in view of further developments in experimental studies and scientific approaches for exposure modelling on the basis of the experiences throughout Europe, in registration of biocidal products.

Partners in the project

1. TNO Chemistry, Netherlands (project co-ordination)
2. Kuopio Regional Institute of Occupational Health, Finland
3. Health and Safety Executive / Laboratories, UK
4. Institute of Occupational Medicine, UK
5. Bundesanstalt für Arbeitsschutz und Arbeitsmedizin, Germany
6. Rijksinstituut voor Volksgezondheid en Milieu, Netherlands
7. CEFIC representatives from BAYER, Germany, and Rohm & Haas, France

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Warren (2003), in preparation.