5.2. Conclusions: EC perspective

5.2.1. Introduction

This study has provided many useful insights into the strengths and weaknesses of the notification scheme for new chemicals established under Directive 67/548/EEC as amended. The results will be taken into account in the preparation of any future modification to the MPD or "base set" used for the notification or chemicals marketed in quantities in excess of 1 tonne per annum. In addition to the direct benefits which will result from the project, the study also allowed the Commission and the national authorities in the Member States to obtain a better understanding of the PMN system as applied in the United States under TSCA. While the benefits which accrue from such improvements in mutual understanding are less tangible and difficult to quantify, they are nonetheless real and will certainly facilitate the development of a more global approach to chemicals control in-line with the objectives set out in Chapter 19 of Agenda 21 of UNCED.

5.2.2. Synopsis

5.2.2.1. Physico-chemical end-points

Of the three end-points which were adequately explored, the SAR methods performed best in relation to log P_{ow}. However, even for this end-point, the predictive methods could not be used with confidence for all chemical groups. Given the relatively low cost of carrying out these tests, the results of this project do not constitute a persuasive argument for introducing SAR into the "base set" as an alternative to testing.

5.2.2.2. Biodegradation

The SAR methods performed extremely well in relation to this end-point, and at the next revision of the "base set", consideration should be given to allowing, under defined conditions, the estimation of biodegradation using SAR.

5.2.2.3. Health effects

The SAR methods are not sufficiently developed in relation to the estimation of eye/skin irritation or sensitisation. As knowledge about these end-points is an essential part of the EC notification scheme, testing for these parameters will continue. SAR techniques were, in contrast, relatively successful in providing qualitative assessments of acute lethal toxicity, and the opportunity for building SAR into a future battery of approaches - including SAR, in vitro tests and non LD50 animal tests - should be explored.

While the SAR methods displayed a tendency to underestimate sub-chronic 28-day, repeated dose toxicity, in most cases this involved an underestimate of the severity of the effects rather than true, "false negatives". At the present time, it is unlikely that the testing requirements for sub-chronic/repeated dose toxicity in the "base set" will be modified. However, it is clear that the SAR techniques provide an excellent additional tool for informing decisions about further testing either immediately post "base set" or at level 1/level 2, as foreseen in the Directive.

With regard to mutagenicity, the results of this project would suggest that SAR could, in a future revision of the "base set", usefully be incorporated into a battery of approaches for evaluating the mutagenic potential of a new chemical. In particular, the issue of the apparent 'false negatives' given by the current "base set" testing package needs to be addressed.

The proportion of substances in the test sample which were predicted as being of concern in relation to end-points not covered by the 6th Amendment "base set", e.g. reproductive toxicity, developmental toxicity, carcinogenicity and neurotoxicity is a considerable source of disquiet. The 7th Amendment to the Directive does foresee the introduction into the "base set" of a screening test for reproductive toxicity. In the light of this project, consideration should also be given to addressing the other "missing" end-points.

5.2.2.4. Ecotoxicity

The SAR methods performed extremely well in predicting acute toxicity to fish and daphnia. They also provided estimates of toxic effects e.g. algal toxicity, not addressed in the "base set" of the 6th Amendment. As part of any future revision, the conditions under which SAR predictions of acute toxicity to aquatic organisms could be integrated into the "base set", should be explored.

5.2.3. Overview

As indicated in the preceeding section, this project has identified a number of possibilities for making greater use of SAR as part of the "base set" testing package applied to new chemicals marketed in the European Community. These possibilities will be explored in the preparation of any future revision to the legislation. However, in contemplating any such revision, there are a number of factors which should also be taken into account.

1) The EC system is operated in a decentralized manner across 12 different national authorities: this figure will shortly be increased to 16 when the EFTA countries join the scheme in the context of the Enlarged European Economic Area. This means that any approach to notification has to be transparent and objective. Thus, while some SAR methods may be used successfully by a group of highly skilled experts working together over many years in one Agency, such an approach could not work in the decentralized system applied in the EC. This means that opportunities for the (consistent) systematic introduction of SAR into the EC scheme could only be considered where the predictive models could be applied objectively by all agencies working within the decentralised system.

2) The EC Directive puts great importance on the classification of a chemical. The emphasis given to classification is frequently misunderstood because the term classification is almost invariably linked with the term labelling, thereby giving the impression that labelling is the only purpose for which substances are classified : this impression is entirely false.

   Classification means the allocation of a substance to one of a number of danger categories on the basis of its intrinsic properties. The decision to allocate substances to a particular category is based on a series of agreed and published criteria. Classification is therefore synonymous with the term hazard/risk identification. Within the EC, classification is consequently the foundation for hazard assessment and the recently agreed Commission Directive laying down the general principles for the risk assessment of new chemicals, recognises classification as providing the starting point for hazard/risk assessment. Secondly, classification may also be the basis for risk reduction: substances classified as carcinogens under the EC scheme are for

example subject to severe restriction in the work place under separate EC legislation. Finally, classification is also the basis for the system of hazard communication by means of standardized labels which has been developed in the EC.

Given the critical importance of classification for the entire EC policy on chemicals, it is essential that the current approach to classification on the basis of objective, transparent criteria is not put into question by allowing the possibility of using SARs instead of test data. Essentially this would mean that SARs could be only admitted :

- if they were objective and reliable and
- if they were able to generate precise quantitative estimations/predictions of test results which could be incorporated into classification schemes or
- if notifiers accepted the principle that classification on the basis of SARs would be admitted but escape from classification i.e. non-allocation to a danger category would not be allowed.

3) The EC notification scheme is directed towards the substance as marketed, including impurities but excluding separable solvents and any non essential stabilizers. The notification scheme is not concerned with purified substances nor is it concerned with formulated products (preparations). While it is clear that the SARs used in this study have in many cases performed very well, such predictive models are in the most part, based upon pure substances. For SARs to be used in a systematic way in the context of the EC notification scheme would require this important issue of impurities to be addressed.