

# The EU REACH Scheme for Chemicals Testing - a Challenge and an Opportunity for Alternatives to Laboratory Animals

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In February 2001, the European Commission (EC) issued a White Paper entitled *Strategy for a Future Chemicals Policy*.<sup>1</sup> This proposed the establishment of a new system called REACH (Registration, Evaluation and Authorisation of CHemicals) to harmonise the safety assessment of both existing and new chemical substances. In May 2003, the EC issued a further set of proposals on REACH,<sup>2</sup> and officially approved the legislation on October 29 2003, while issuing the final draft of the legislation, in six volumes<sup>3</sup>.

While a unified testing system for chemicals is sensible, the underlying policy is ill-conceived because it: a) is based on the unrealistic concept of a risk-free environment; and b) fails to define how non-animal approaches should be implemented, while generally promoting their usage. REACH is based on a top-down approach, in which the information required is dictated by production volume (tonnage). This assumes erroneously that the higher the level of production of a substance, the greater the level of human exposure.

## Implications for using laboratory animals

Many laboratory animals could be required if REACH is based on check-list toxicity testing, and dictated by a tonnage-trigger system, rather than by more-pertinent measures of likely exposure, such as bioavailability. This would cause substantial ethical, scientific and logistical problems, especially for industry<sup>4</sup>, that would be incompatible with the time-schedule envisaged for testing. The legislation includes several suggestions for minimising animal testing, but the text of the policy is ambiguous in places<sup>5</sup>. Moreover, the EC has included the OECD Health Effects Test Guidelines (TGs) in one of the Annexes to REACH. This merely reproduces TGs mostly for animal tests ignoring several approved alternative methods,

implying that the original guidelines are intended to be used. FRAME has found much scope for improving these TGs for their application to REACH.

To speed up testing and to avoid duplication, it would be preferable for data to be shared and published as part of the new policy. This is advocated by the EC, but is not a legal obligation, and raises important confidentiality issues.

## Strategies for using non-animal approaches in REACH

Of the testing schemes that have been proposed<sup>5</sup>, some are very general, eg the European Centre for the Ecotoxicology and Toxicology of Chemicals (ECETOC) and the Royal Commission on Environmental Pollution (RCEP) schemes. Only proposals produced by the BUAV and FRAME<sup>6</sup> directly address how non-animal approaches could be integrated into a testing strategy. An EC scientific committee<sup>7</sup> has, however, indicated its lack of support for the BUAV suggestions, reaffirming its commitment to animal testing.

The FRAME tiered scheme<sup>6</sup> (fig 1) is intended to facilitate efficient evaluation of chemicals for human and environmental hazard, while minimising the use of laboratory animals. It starts with preliminary risk assessment (involving available information), followed by testing,

based on physicochemical properties and (Q)SAR approaches. The latter are used with expert system and biokinetic modelling, and information on metabolism, to identify key metabolites and bioavailability. These data, with production levels and patterns of use, are used to assess potential exposure. Further testing should be dictated strictly by a need to fill essential information gaps, and should rely on non-animal methods, as far as possible. The scheme includes a feedback loop, so that new data are used to improve the predictivity of prediction systems.

## Discussion

Our strategy is based on the principles that: a) testing should only be initiated when useful human exposure information is available; b) exposure should be determined by bioavailability, then patterns of use and production levels; and c) after preliminary risk assessment, any further testing should avoid duplication, should include any pre-existing data, should be driven by a justifiable need for data, and should be flexible. Thus, animal testing will only need to be a last resort.

There are similarities between our proposals and those made by the RCEP,<sup>6</sup> especially the call for increased usage of computational prediction methods. However, FRAME recognises that it is not a simple matter of adopting practices in the

pharmaceutical industry. Thus, for (Q)SAR models to be used not only for screening but also to generate definitive hazard data for risk assessment, they need to be formally validated for reliability and relevance.

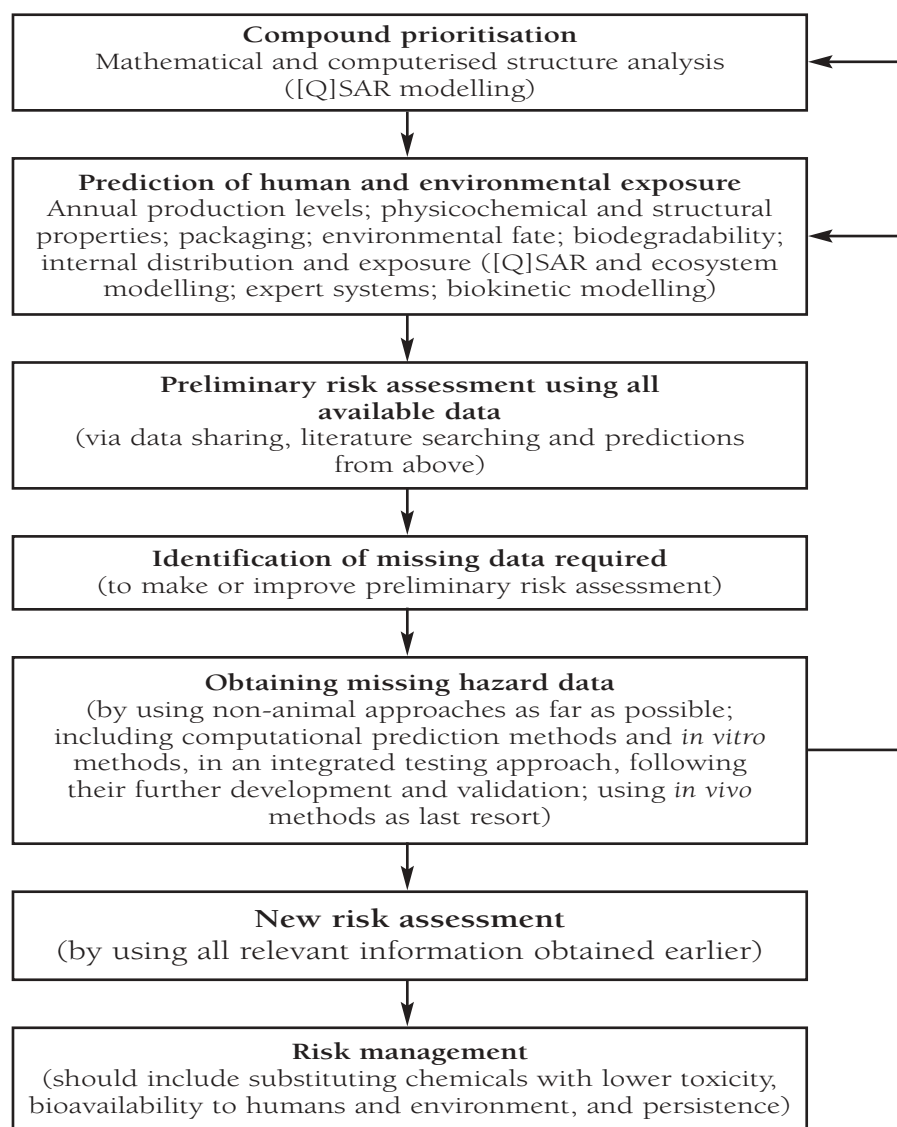
## Conclusions

FRAME makes the following recommendations: a) the EU should only require testing of chemicals where there is adequate evidence of exposure to humans or wildlife; b) the EU should maximise the application of *Directive 86/609EEC* (requiring the use of alternatives whenever possible), by waiving requirements for animal tests at the registration stage, in favour of validated *in vitro* test methods, as soon as they become available; and c) new initiatives for developing and validating non-animal approaches for safety assessment should be established.

A fresh approach to assessing the risk of exposures to chemicals is desperately needed. The advent of the REACH policy, while being a huge challenge for the development of alternatives, is also an ideal opportunity to reassess our reliance on hazard data based on outdated, and often imprecise, animal testing and inadequate information on exposure. It is time to consider how best to use data from more modern non-animal methods that can permit extrapolation from effects on (human) cell cultures to whole organisms and populations. It is hoped that there is time to improve REACH by further consultation.<sup>8</sup>

## References

- <sup>1</sup>Anon. (2001). White Paper on a Strategy for a Future Chemicals Policy (COM(2001)88 final). Web site <http://europa.eu.int/comm/environment/chemicals/whitepaper.htm>
- <sup>2</sup>Anon. (2003). European Commission website [http:// europa.eu.int/comm/enterprise/ chemicals/chempol/whitepaper/reach.htm](http://europa.eu.int/comm/enterprise/chemicals/chempol/whitepaper/reach.htm)
- <sup>3</sup>European Commission (2003). Consultation Documents Volumes I–VII Concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). Website <http://europa.eu.int/comm/ environment/chemicals/whitepaper.htm>
- <sup>4</sup>Weller, J.L. & Bidstrup, W.R. (2003). Scope and potential impact of the EU's new 'REACH' chemical proposal. *PharmaChem* 2, 50-55.
- <sup>5</sup>Dandrea, J. & Combes, R.D. (2003). A survey of stakeholder organizations on the proposed new European chemicals policy. *ATLA* 31, 501-528.
- <sup>6</sup>Combes, R.D., Dandrea, J. & Balls, M. (2003). FRAME and the Royal Commission on Environmental Pollution: common recommendations for assessing risks posed by chemicals under the EU REACH system. *ATLA* 31, 529-535.
- <sup>7</sup>Anon (2004). Opinion of the Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE) on the BUAV-ECEAE Report on 'The Way Forward – Action to End Animal Toxicity Testing, European Commission, Health & Protection Directorate-General, Brussels, C7/VR/csteeop/ anat/080104 D(04).
- <sup>8</sup>Anon (2004). UK Consultation paper on the new EU chemicals strategy. <http://www.defra.gov.uk/corporate/consult/reach/index.htm>



*Incorporating ideas from the Royal Commission on Environmental Pollution report and modified from (6), the scheme includes a feedback loop for hazard data to be used to improve computational prediction methods.*

**(Q)SAR** = (quantitative) structure-activity relationship.

**REACH** = Registration, Evaluation and Authorisation of Chemicals.

**Figure 1: The FRAME decision-tree testing scheme for REACH**