

Assuring Safety without Animal Testing: New Risk Assessment Approaches for Skin Allergy and Cancer



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Background

Assuring the safety of consumer products without the need to conduct animal tests on their ingredients is a considerable challenge. In 2004, Unilever published a **novel conceptual framework** for making consumer safety decisions that could potentially enable animal tests to be replaced. This framework is focused on the development of new risk assessment approaches that will allow the integration and interpretation of non-animal data. Our on-going research activities aim to explore the feasibility of these new approaches.

Risk-based Safety Assurance

No substance, process or activity is completely hazard free, so finding out that something is hazardous does not tell you whether it is safe.

Risk assessment is the science of determining the likelihood that a hazard will be expressed. **Unilever's approach to safety assurance is therefore risk rather than hazard based.** This means that when performing a safety assessment, the extent and level of exposure, the type of ingredient, and all available data are used to judge the level of risk associated with an ingredient in use. This process starts before any experimental work commences and helps to avoid unnecessary testing and ensure studies that are performed are relevant to the safety assessment.

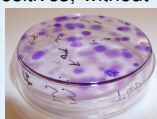


New Risk Assessment Approaches

Cancer

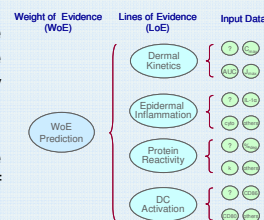
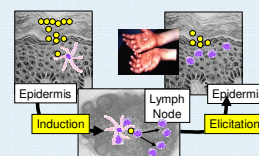
The use of *in vitro* tests (in the 'test tube' rather than in animals) to screen out chemicals likely to cause cancer in humans, is a particular success story in toxicology alternatives. However, it is difficult to use current *in-vitro* assays in a risk assessment context. Furthermore, current tests, using mammalian cells in culture, suffer from an unfavourably high *irrelevant positive rate*. This means that safe new chemicals can be wrongly rejected as potential carcinogens. The Unilever research effort is seeking to:

1. Improve the current mammalian cell assays and implement more effective and earlier screening with advanced tests, teamed with computational predictor methods.
2. Develop new tests for follow up to frontline-test positives (distinguishing the true from the irrelevant positives, without recourse to animal tests) including:
 - a. Cell transformation assays utilizing new biological endpoints
 - b. Three-dimensional human skin models.
3. Generate new biological insights into the development of skin cancer, using a palette of new technologies (including metabolomics, transcriptomics, proteomics, genomic phenotyping, IR-microspectroscopy and systems biology modelling).
4. Integrate data into novel risk assessments, including the evaluation of thresholds, the influence of reactive oxygen species (free radicals) and exposure/dose considerations.

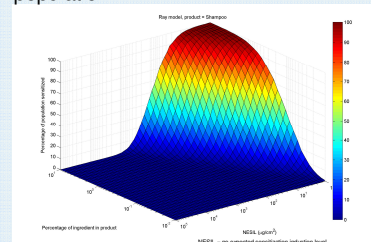
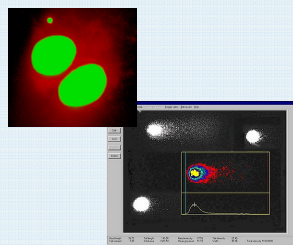
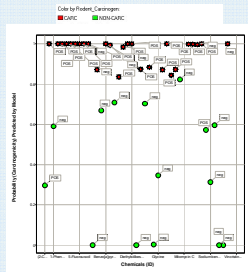


Skin Allergy

Accurate hazard characterisation is often required for skin allergy risk assessment. The biology of skin allergy is complex and involves interactions (many unknown) between different cell types across a number of different sites within the body. With current technology, the replication of these interactions in a single *in vitro* system is not yet possible. Nevertheless, *in vitro* techniques can be used to assess the activity of the major contributing pathways of the disease. Unilever is currently investigating the experimental feasibility of these techniques and methods with which to integrate the resultant data as a possible means of non-animal hazard characterisation for risk assessment of skin allergens.



Not everyone reacts in the same way to a skin allergen. Whether someone suffers an allergic reaction depends on many variables, for example how they use the product and where it is applied, and the susceptibility of the individual to developing allergic skin disease. This susceptibility may be affected by different factors, including age and skin condition. We are currently working to increase understanding of the range of these variables. Our aim is to ultimately include these considerations in a statistical tool that will ensure our risk assessments are more explicit about this variation in the population.



The output of a statistical tool to predict the percentage of a population that could be affected by an allergen present in a shampoo. The feasibility of using non-animal data to run this model is under investigation.

Part of Unilever's ongoing effort to develop novel ways of delivering consumer safety.

This work has been performed by several teams within Unilever and in collaboration with the following external partners: Barts and The London School of Medicine and Dentistry, UK; BioFocus DPI, UK; BioReliance, USA; Charles River Laboratories, UK; Entelos Inc., USA; Imperial College London, UK; Information Network of Departments of Dermatology (IVDK), Germany; Kings College London, UK; Lancaster University, UK; Massachusetts Institute of Technology, USA; Oroxcell, France; ProBioGen, Germany; University of Cambridge, UK; University of Liverpool, UK; University of Manchester, UK; University of Nottingham, UK; University of Pittsburgh, USA; University of Southampton, UK