



## Eliminating Testing Involving Animals - Our Recent Contributions



At P&G we believe the **elimination** of animal testing is the right thing to do.



We do not test on animals unless required by law. We will continue to develop non-animal alternative tests and work with regulators around the world to ultimately end research involving animals.

## **Our commitment drives progress**

**We have developed over 50 non-animal testing methods** and invested more than \$350 million in finding alternatives.

One result of this investment is the development of the first non-animal alternative to skin allergy tests to be approved by European authorities, a major mile-stone for product safety research.

**We partner with leading animal protection groups**, such as the Humane Society of the United States (HSUS) and the American Society for the Prevention of Cruelty to Animals (ASPCA), to promote alternative research methods and enhance animal welfare.

“The Humane Society of the United States has worked with P&G scientists for over 20 years to successfully change animal testing regulations and practices. One of the key barriers to eliminating animal testing is the acceptance of non-animal alternative tests by government regulators. P&G plays a leading role in developing alternatives to animal testing and promoting their acceptance. Advances in technology and science are providing the basis for new safety assessments. Eliminating animal testing is an ambitious goal. But by working together, animal protection groups and committed corporations can make it happen.”



**Andrew N. Rowan**  
*Chief Scientific Officer*  
*Humane Society of the United States*

## Better Science

The elimination of animal testing is not only more humane and better business practice, it's also better science.

“Here at P&G, we're committed to every approach that can lead us to eliminating research involving animals. If one approach doesn't work, we keep trying until we find something that does. Alternative tests are humane and often more accurate than testing with animals. They are our number one choice.”



**Petra Kern**  
*PhD, Principal Scientist*



Alternate tests  
are often more  
**effective**



## Transforming Skin Allergy Tests

In 2014, the first ever non-animal alternative to skin allergy tests was officially approved by European authorities. This test, known as DPRA (Direct Peptide Reactivity Assay), was invented by P&G. Skin allergy is a complex process and an important safety test for almost all ingredients. As a result, this alternative marks a milestone in overcoming the need for animal testing.

In this new test, ingredients are added to small test tubes and their potential to react with peptides, mimicking skin proteins, are measured. The test shows if an ingredient is a potential allergen and whether it poses a safety risk. The DPRA has now received official endorsement and P&G is rolling it out across the business to replace research involving animals wherever possible.

**“We know that the development of alternative tests, from initial idea to acceptance by government authorities, can be a challenging and lengthy process. As a result, we are incredibly pleased that the DPRA has received the final official recommendation from a group of independent authority experts.”**



**Frank G. Gerberick**  
*PhD, Director and P&G Victor Mills Society member*

In addition to this work P&G, together with outside experts, has conducted extensive research into how the skin transforms ingredients. We have been able to identify skin cell cultures and models that imitate what happens as an ingredient passes through the skin.

**“As a result, we are now using test tubes and cell cultures, rather than new animal data.”**



**Carsten Goebel**  
*PhD, Research Fellow*

## Pushing the boundaries, a new approach to skin models

For many years scientists have used non-animal test tube experiments with mammalian cells and bacteria to screen for potentially harmful ingredients. However, these test tube or in vitro experiments often create false alerts, leading to unnecessary follow up research with animals for ingredients that in reality aren't harmful.

In response, P&G, with Cosmetics Europe, the European Cosmetics Trade Association, has developed a new cutting edge test using artificial skin, to act as a direct replacement for animal studies. These tests, which are currently undergoing validation, use three dimensional human skin generated from cells donated by human volunteers.

**“At P&G we hope this work, like all our other research into alternatives, will transform safety tests and help to eliminate research involving animals completely.”**



**Stefan Pfuhler**  
*PhD Principal Scientist*

## Revolutionizing eye irritation tests

A key function of all safety assessments is to prevent harm from accidental eye contact. Due to our commitment to replacing animal tests, P&G evaluates eye irritation using alternatives such as cell culture tests and reconstructed human tissue, eliminating the need for animals in this research.

A cornerstone of our work in this area has been to participate in, and in some instances lead, industry activities.

**“We work to optimize in vitro tests and extend their applicability to all types of ingredients and to secure regulatory acceptance.”**



**Pauline McNamee**  
*PhD, Principal Scientist*

## Making the most of existing data

While test tube experiments are transforming the work of global scientists and regulators, there are still areas where further research is needed before sufficient alternative test methods can replace animal tests. If we are to end the use of animals in research completely we must go beyond in vitro tests. For areas where a set of non-animal alternative tests are not yet available, scientists must make the most of existing data.

For many years, scientists around the globe have tried to assess the safety of ingredients with computer models, building on existing data from similar substances. But without clear guidance and frameworks it is hard to make the most of this information, and unnecessary tests are often repeated.

To address this issue P&G has created a framework that pairs untested ingredients with ingredients that have the same or similar molecular structures (analogs), which already have well established safety profiles and can therefore be deemed safe. To make this framework as simple as possible P&G has given each analog a rating for its suitability alongside an expert evaluation.

**“Having compiled the data, we published and shared the framework as widely as possible, promoting both its use and regulatory acceptance.”**



**Karen Blackburn**  
*PhD, Research Fellow*



## Sharing science

We want other researchers and manufacturers to benefit from our advances, so that everyone can end product safety research using animals. We've shared our alternatives research in more than 400 scientific publications and routinely present our findings at scientific meetings and workshops.

In addition P&G has developed a platform of legacy data and shared information via a new database. This allows us to predict the long term safety of cosmetic ingredients and to optimise safety assessments. This freely available public resource collates and curates both historical and unpublished research from industry, universities and Governmental Organizations, previously unavailable to the wider scientific community. As part of this project jointly funded by the EU Commission and Cosmetics Europe (the trade association of European cosmetics manufacturers) we have collaborated with industry experts, independent scientists and the EU Commission.

**"As more data is contributed and the platform grows, so will the efficacy of our predictions."**



**Catherine Mahony**  
*PhD, Principal Scientist*



## Advancing Technology

Technology advancements have enabled P&G to dramatically reduce the need for regulatory mandated animal testing.

We know these tests work. We continue to invest in promising new areas of research that provide a more complete picture of how cells respond to ingredients to make safety assessments more efficient and precise. We're also investigating the latest thinking in the following areas of modern science:

- **Genomics** – Genetic mapping and DNA sequencing
- **Proteomics** – Using genetics to analyze proteins
- **Metabolomics** – Studying unique metabolic patterns of substances
- **Bioinformatics** – Solving molecular biological problems with mathematics, informatics, statistics, computer science, artificial intelligence, chemistry, and biochemistry

We are **reducing**  
the need for animal  
testing



## Working with external partners

We work closely with governments around the world to develop and validate alternative testing methods. We encourage regulations that require research involving animals to be eliminated wherever possible. For example, we're currently working with the U.S. Environmental Protection Agency (EPA) to remove required animal tests for disinfectants.

We also collaborate with respected governmental and non-governmental organizations and leading animal protection groups to raise awareness of the many existing alternatives. Our partners include:

### **The Humane Society of the United States (HSUS)**

The largest animal protection organization in the United States, HSUS is a non-profit that works to protect all animals through legislation, litigation, investigation, education, advocacy and field work. [www.hsus.org](http://www.hsus.org)

### **The European Consensus-Platform for Alternatives (ecopa)**

An international non-profit, ecopa brings together national consensus platforms on alternative methods, including animal welfare groups, industry, academia and governmental institutions. [www.ecopa.eu](http://www.ecopa.eu)

### **The Institute for In Vitro Science (IIVS)**

A non-profit organization dedicated to the advancement of alternative testing methods, IIVS seeks to refine the science, broaden the use, and increase the acceptance of in vitro testing worldwide. [www.iivs.org](http://www.iivs.org)



“Through collaboration and partnerships, we can share **knowledge** and end requirements for animal tests”

### **Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)**

Made up of representatives from 15 U.S. federal regulatory and research agencies, ICCVAM promotes the regulatory acceptance of toxicological test methods that reduce, refine and/or replace animal use. [www.iccvam.niehs.nih.gov](http://www.iccvam.niehs.nih.gov)

### **European Union Reference Laboratory for alternatives to animal testing (EURL ECVAM)**

Hosted by the Joint Research Centre, Institute for Health and Consumer Protection, EURL ECVAM was set up to respond to the increasing need for new methods to be developed and proposed for validation in the European Union.

[http://ihcp.jrc.ec.europa.eu/our\\_labs/eurl-ecvam](http://ihcp.jrc.ec.europa.eu/our_labs/eurl-ecvam)

### **The European Partnership for Alternative Approaches to Animal Testing (EPAA)**

A joint initiative of the European Commission, companies, and trade federations, EPAA works to promote the development of new '3R' methods (refine, reduce, replace) as modern alternative approaches to safety testing. [www.epaa.eu.com](http://www.epaa.eu.com)

### **[www.AltTox.org](http://www.AltTox.org)**

A website sponsored and supported by P&G, dedicated to advancing non-animal methods of toxicity testing through online discussion and information exchange.

## Influencing Regulation

We only test on animals when required by law.

Various laws in the United States, Canada, the EU and some countries in Asia and Latin America still require specific animal tests to determine safety for certain products or ingredients, even though alternatives are often available.

In other cases, alternative tests are accepted in some countries but not in others. We support changes in laws and regulations around the world to reduce and, eliminate unnecessary animal testing.

## Changing safety assessment approaches globally

While some regulators accept safety assessments on the basis of individual ingredient profiles, others still insist on finished product tests.

In line with our objective to stop testing involving animals completely, P&G is working with governments around the world to change approaches to safety tests and in particular, advocate for ingredient-based risk assessments.

Since 2010 P&G has run seminars tailored to the needs of regulators involved in the design and the application of cosmetic regulations, e.g. in China, offering the opportunity for dialogue and discussion on testing approaches. As a result, change is already underway. In 2014 cosmetic legislation for a number of products in China was revised, allowing the use of ingredient based, non-animal alternative safety assessments.



## Promoting alternatives

We help educate policymakers about new alternatives for evaluating product safety. We are working with governments and other organizations to align regulations wherever possible.

We also work with trade associations such as the European Cosmetics Trade Association Cosmetics Europe, and the US Personal Care Products Council (PCPC), as well as academic organizations, to promote alternatives.

We have organized animal alternatives workshops in Moscow and Beijing to foster discussion in emerging markets about new tests.

P&G was a sponsor of each of the eight World Congresses on Alternatives and Animal Use in the Life Sciences and is again Platinum Sponsor of the 9th World Congress in 2014. These events provided opportunities for researchers to share information, and for our scientists to present the latest animal alternative testing discoveries.

We are working to **harmonize** regulations concerning alternatives



# P&G's Record of **Commitment**

## **Four decades of making a difference.**

P&G has been actively pursuing animal alternatives for nearly 40 years.

### **1970s**

P&G was one of the first companies to put safety testing data into a computer database, helping to avoid duplicate testing.

### **1980s**

P&G recruited scientists and invested in state-of-the-art laboratories to build a research organization dedicated to reducing and eliminating the use of animals in research.

### **1989**

P&G established a program to award research grants to develop animal testing alternatives.

### **1990**

P&G helped fund the first International Conference on Validation. P&G also joined the National Institute of Health and Animal Rights International, co-sponsoring research on sharing data for product testing.

### **1991**

P&G testified before the U.S. Congress to support legislation to promote alternatives research and to establish criteria for regulatory acceptance of alternatives.

### **1992**

Johns Hopkins Center for Alternatives to Animal Testing recognized P&G for "outstanding contributions in finding alternatives" in product development and safety evaluations.

### **1993**

P&G was a sponsor of the first World Congress on Alternatives held in Baltimore, Maryland.

### **1997**

P&G joined other organizations, including the Humane Society of the United States (HSUS), in helping fund the launch of Altweb, a website resource on alternatives research and validation activities.



**1998**

P&G testified before the U.S. Congress to support legislation to accelerate the acceptance of alternative tests.

**1999**

P&G ended the use of animals in safety testing for its consumer products except when non-animal research alternatives are not available. The HSUS presented its prestigious Russell and Burch Award to a P&G Research Director in recognition of her work and leadership in advancing alternatives research.

**2002**

The HSUS presented its Humane Award to P&G in recognition of the company's efforts to make the world a better place for animals.

**2003**

Iams established an independent animal care advisory board to provide expert advice on animal care standards in nutritional feeding studies.

**2005**

The HSUS and P&G announced a strategic partnership to work together to eliminate testing involving animals for consumer product safety.

**2005**

P&G provided funding for a senior P&G scientist to work directly with ECVAM to foster the validation of alternative methods, and to advocate for their acceptance by regulatory agencies.

**2007**

The website AltTox.org was launched through a collaboration with P&G and HSUS. The website is dedicated to advancing non-animal methods of toxicity testing.

**2009**

P&G presented 22 research papers on animal alternatives and animal welfare topics at the 7th World Congress on Animal Alternatives in Rome, Italy. The DPRA (Direct Peptide Reactivity Assay) was submitted for official validation studies.

**2011**

P&G sponsored the 8th World Congress on Animal Alternatives in Montreal, Canada.

**2012**

The official validation study of the DPRA (Direct Peptide Reactivity Assay) was successfully published.

**2013**

P&G's DPRA (Direct Peptide Reactivity Assay) a ground-breaking alternative skin allergy test was finally officially approved and recommended by a key regulatory authority.

**2014**

P&G sponsored the 9th World Congress on Alternatives and Animal use in Life Science in Prague. P&G has sponsored each World Congress on Animal Alternatives.

## Our policy

At P&G we believe the elimination of animal testing is the right thing to do.

P&G does not test its products or ingredients on animals anywhere in the world, unless required by law.

We will continue to work with outside scientists and governments to develop alternatives to animal testing, which we believe is the only way to overcome the need for animal testing globally.

As a matter of policy we comply with all relevant regulations in every market in which we operate.

## Where next?

While a lot has been achieved to end the use of animals in research, the scientific and regulatory communities are not there yet.

Not all global regulators and authorities accept or make the broadest use of the alternatives currently available. While in some safety areas, accepted alternatives do not exist yet.

We will continue our research efforts and work with the global scientific community until this issue is resolved and alternatives are available for all relevant safety questions, meeting the needs of government regulators across the globe.



## Footnotes

<http://www.cosmeticsdesign-europe.com/Formulation-Science/P-G-develops-first-approved-non-animal-alternative-for-skin-allergy-testing>

[http://hcp.jrc.ec.europa.eu/our\\_labs/eurl-ecvam/eurl-ecvam-publishes-recommendation-dpra](http://hcp.jrc.ec.europa.eu/our_labs/eurl-ecvam/eurl-ecvam-publishes-recommendation-dpra)

Gerberick, G. F., Troutman, J. A., Foertsch, L. M., Vassallo, J. D., Quijano, M., Dobson, R. L., Goebel, C., and Lepoittevin, J. P., 2009. Investigation of Peptide Reactivity of Pro-hapten Skin Sensitizers Using a Peroxidase-Peroxide Oxidation System. *Toxicol Sci* 112, 164-174.

Goebel C, Hewitt NJ, Kunze G, Wenker M, Hein DW, Beck H, Skare J. Skin metabolism of aminophenols: human keratinocytes as a suitable in vitro model to qualitatively predict the dermal transformation of 4-amino-2-hydroxytoluene in vivo. *Toxicol Appl Pharmacol*. 2009 Feb 15;235(1):114-23

Pfuhler S, Fautz R, Ouedraogo G, Latil A, Kenny J, Moore C, Diembeck W, Hewitt N.J, Reisinger K, Barroso J. (2014): The Cosmetics Europe strategy for animal-free genotoxicity testing: Project status up-date. *Toxicology in Vitro*, 28 (1), pp. 18-23

Pfuhler S, Kirst A, Aardema M, Banduhn N, Goebel C, Araki D, Costabel-Farkas M, Dufour E, Fautz R, Harvey J, Hewitt NJ, Hibatallah J, Carmichael P, Macfarlane M, Reisinger K, Rowland J, Schellau F, Schepky A, Scheel J (2010): A tiered approach to the use of alternatives to animal testing for the safety assessment of cosmetics: Genotoxicity. A COLIPA analysis. *Regulatory Toxicology and Pharmacology*, 57 (2-3), pp. 315-324

Pfuhler S, Fautz R, Ouedraogo G, Latil A, Kenny J, Moore C, Diembeck W, Hewitt N.J, Reisinger K, Barroso J. (2014): The Cosmetics Europe strategy for animal-free genotoxicity testing: Project status up-date. *Toxicology in Vitro*, 28 (1), pp. 18-23

Aardema MJ; Barnett BC; Khambatta Z; Reisinger K; Ouedraogo-Arras G; Faquet B; Ginestet AC; Mun GC; Dahl EL; Hewitt NJ; Corvi R; Curren RD: International prevalidation studies of the EpiDerm 3D human reconstructed skin micronucleus (RSMN) assay: transferability and reproducibility. *Mutat Res*.

Hewitt N, Edwards, R.J, Fritsche, E, Goebel, C, Aebly, P, Scheel, J, Reisinger, K, Ouedraogo, G, Duche, D, Elstein, J, Latil, A, Kenny, J, Moore, C, Kuehnl, J, Barroso, J, Fautz, R, Pfuhler, S (2013): Use of human in Vitro skin models for accurate and ethical risk assessment: Metabolic considerations. *Toxicological Sciences*, 133 (2)

Reus, A.A., Reisinger, K., Downs, T.R., Carr, G.J., Zeller, A., Corvi, R., Krul, C.A.M., Pfuhler, S. (2013): Comet assay in reconstructed 3D human epidermal skin models-investigation of intra- And inter-laboratory reproducibility with coded chemicals. *Mutagenesis*, 28 (6), pp. 709-720

SCCS/1532/14: Scientific Committee on Consumer Safety (SCCS): ADDENDUM to the SCCS's Notes of Guidance (NoG) for the Testing of Cosmetic Ingredients and their Safety Evaluation, 8th Revision (9 April 2014)

Blackburn, K. and S. Stuard. 2014. A Framework to Facilitate Consistent Characterization of Read Across Uncertainty. *Regulatory Toxicology and Pharmacology* 68: 353–362

OECD, 2007. OECD Guidance on Grouping of Chemicals, Paris

Blackburn, Karen, Donald Bjerke, George Daston, Susan Felter, Catherine Mahony, Jorge Naciff, Steven Robison and Shengde Wu. 2011. Case studies to test: A framework for using structural, reactivity, metabolic and physicochemical similarity to evaluate the suitability of analogs for SAR-based toxicological assessments. *Regulatory Toxicology and Pharmacology* 60: 120-135

Blackburn, K. and S. Stuard. 2014. A Framework to Facilitate Consistent Characterization of Read Across Uncertainty. *Regulatory Toxicology and Pharmacology* 68: 353–362

Wu, Shengde, Karen Blackburn, Jack Amburgey, Joanna Jaworska and Thomas Federle. 2009. A Framework for Using Structural, Reactivity, Metabolic and Physicochemical Similarity to Evaluate the Suitability of Analogs for SAR-based Toxicological Assessments. *Regulatory Toxicology Pharmacol* 56: 67-81

OECD, 2014. Guidance on Grouping of Chemicals, Second Edition

McNamee P, Faller C., Goebel C., Pfuhler S., Sieber T., 2009. Use of HPLC/UPLC instead of photometry for evaluation of MTT in in vitro RhT assays for irritation; assessment of colored materials. ALTEX. 26, special issue: Abstracts 7th World Congress, Rome, 2009. p.281

McNamee, P, Hibatallah, J, Costabel-Farkas, M., Goebel, C., Araki, D., Dufour, E., Hewitt, N., Jones, P, Kirst, A., Le Varlet, B., Macfarlane, M., Marrec-Fairley, M., Rowland, J., Schellau F., Scheel, J., 2009. A tiered approach to the use of alternatives to animal testing for the safety assessment of cosmetics: Eye irritation. *Regulatory Toxicology & Pharmacology*. 54, 197-209

Alépée, N., Barroso, J., De Smedt, A., De Wever, B., Hibatallah, J., Klaric, M., Mewes, K.R., Millet, M., Pfannenbecker, U., Tailhardat, M., Templier, M. McNamee, P., 2014. Use of HPLC/UPLC for Endpoint Detection in In Vitro Reconstructed human Tissue (RhT) Test Methods to Expand Applicability to Strongly Coloured Test Substances. Submitted to *Toxicology in Vitro* 2014

Alépée, N., Bessou-Touya, S., Cotovio, J., De Smedt, A., De Wever, B., Faller, C., Jones, P., LeVarlet, B., Marrec-Fairley, M., Pfannenbecker, U., Tailhardat, M., van Goethem, F., McNamee, P., 2013. Cosmetics Europe multi-laboratory pre-validation of the SkinEthic™ reconstituted human corneal epithelium test method for the prediction of eye irritation. *Toxicology In Vitro*. 27, 619-626

Catherine Mahony, "P&G's approach to data sharing for the Seurat-1 COSMOS project", 9th World Congress on Alternatives and Animal Use in the Life Sciences, Prague, August 2014

