Ending Cosmetic Animal Testing & Trade in Brazil and Worldwide





Expert team

Toxicology, ecotoxicology, pharmacology, regulatory science, endocrinology, biochemistry, neuroscience, law, etc.

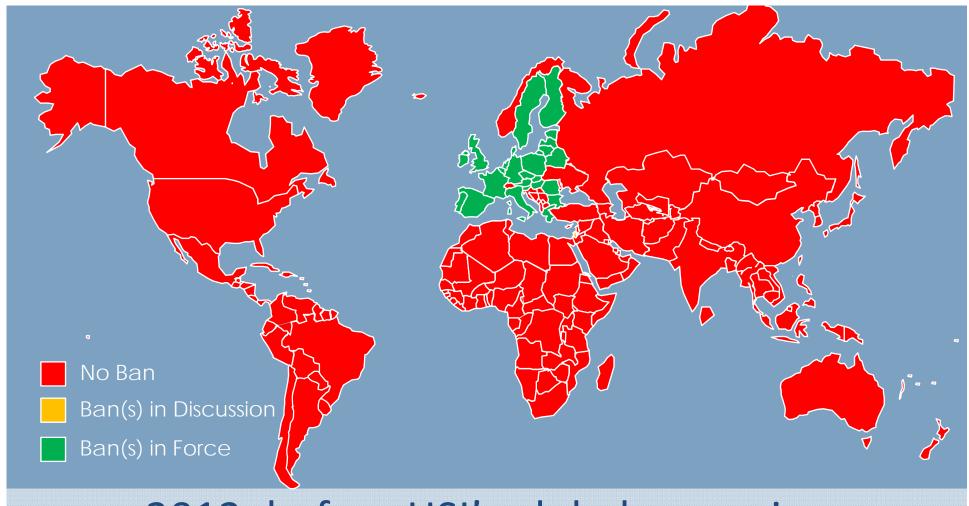
Global presence

Brazil, United States, Canada, Mexico, Central America, European Union, India, Japan, South Korea, Viet Nam, Australia, Africa and beyond

Approach

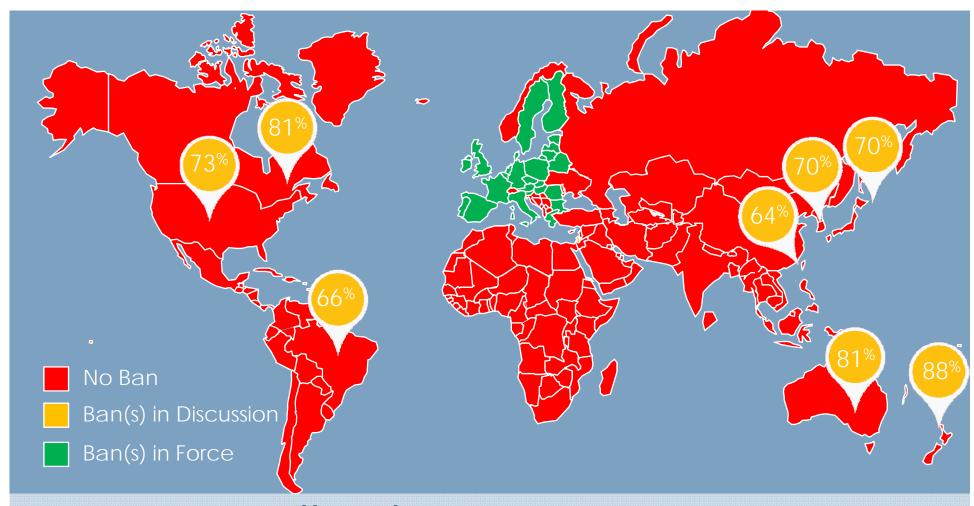
Working with policy makers, regulators, companies, scientists, and other stakeholders to build partnerships for progress

HSI is the leading international NGO working to advance non-animal testing & health research



2012: before HSI's global campaign

EU ban on cosmetic animal testing; sales ban uncertain



Polling by HSI & partners

Public support for cosmetic animal testing ban

The global cruelty-free revolution













2013

• EU – sales ban

• India – test ban

• Brazil - PLC

70/2014

2014



- Brazil São Paulo & Mato Grosso do Sul state test bans
- China ends mandatory animal • Israel – sales ban testing for some domestically produced cosmetics

- New Zealand test ban
- South Korea sales ban (dependent on available alternative methods)
- Turkey mandatory alternatives
- Brazil Paraná & Amazonas state test bans

2016

- Taiwan test ban
- Switzerland test ban
- Brazil Pará state test ban

2017

- Switzerland sales ban
- Guatemala test ban
- Brazil Senate CCT unanimously endorses amendments to PLC 70/2014
- Australia promises to implement dual test + sales ban



2017: after campaigning by HSI and others

37 national testing/trade bans; 10+ others in development





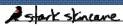




















'Responsible innovation'





- Choose from among thousands of existing ingredients with established toxicity profiles and history of safe use
- Evaluate new product formulations using modern non-animal methods (calculation, computer modeling, cell tests)
- 3. Avoid new-to-the-world chemical ingredients (subject to new animal testing under chemical laws)
- 4. Avoid ingredients with known health concerns that may be subject to further animal testing

Animal tests = last century's science

1920s 1940s 1960s 2017













We embrace new technology in virtually every part of lives...

PAST...







PRESENT...







... so why is cosmetic safety still assessed using tests that are 50-90 years old?

Modern non-animal methods are more predictive, e.g. skin allergy

Regulatory Toxicology and Pharmacology 63 (2012) 489-504



Contents lists available at SciVerse ScienceDirect

Regulatory Toxicology and Pharmacology





Putting the parts together: Combining in vitro methods to test for skin sensitizing potentials

Caroline Bauch a.b, Susanne N. Kolle a, Tzutzuy Ramirez a, Tobias Eltze a, Eric Fabian a, Annette Mehling c.*, Wera Teubner^d, Bennard van Ravenzwaay^a, Robert Landsiedel^a

- ² BASF SE, Experimental Toxicology and Ecology, Ludwigshafen, Germany
 ³ University of Manchester, Faculty of Life Sciences, Manchester, United Kingdom
- ^c BASF Personal Care and Nutrition GmbH, Düsseldorf, Germany ^d BASF Schweiz AG, Basel, Switzerland

ARTICLE INFO

Keywords: Skin sensitization Ell cosmetics regulation Alternative methods Prediction model DPRA KeratinoSens™

ABSTRACT

Allergic contact dermatitis is a common skin disease and is elicited by repeated skin contact with an allergen. In the regulatory context, currently only data from animal experiments are acceptable to assess the skin sensitizing potential of substances. Animal welfare and EU Cosmetic Directive/Regulation call for the implementation of animal-free alternatives for safety assessments. The mechanisms that trigger skin senstitzation are complex and various steps are involved. Therefore, a single in vitro method may not be able to accurately assess this endpoint. Non-animal methods are being developed and validated and can be used for testing strategies that ensure a reliable prediction of skin sensitization potentials. In this study, the predictivities of four in vitro assays, one in chemico and one in silico method addressing three differen steps in the development of skin sensitization were assessed using 54 test substances of known sensitizing potential. The predictivity of single tests and combinations of these assays were compared. These data were used to develop an *in vitro* testing scheme and prediction model for the detection of skin sensitizers based on protein reactivity, activation of the Keap-1/Nrf2 signaling pathway and dendritic cell activation. © 2012 Elsevier Inc. All rights reserved.

1. Introduction

As the interface between the environment and the body, the skin is continuously exposed to environmental insults, pathogens

Abbrevations: ARE antioxidant response element: AUC area under the curve: C.C., control cells; CV75, concentration reducing viability to 75%; DC, dendritic cells; DMSO, dimethyl sulfoxide; DNCB, 1-chloro-2,4-dinitrobenzene; DPRA, Direct DMSO, dimethyl sulfouide: DNSB, 1-chiero-2-d-dinitrobenzene: DPRA, Direct Peptide Restrivity Assay; EUAR, Lorgopan Chemica Branço; EXVAM, European Cemire for the Validation of Atternative Methods; PBS, feath bornes serum; FITI, and present the control of the Company of the Co mixtur of 5-diloro-2-methyl-4-isothization-3-one and 2-methyl-4-isothization-3-one; MFI, mean funditivity MTI, 34(4-3-dimethylthizatio-2-yly-2-diphenyl tetrazoitum bromide; mMUSST; modified myeliod US97 dendritic cell activation-based six mestitization to (S.) KDPH; nicitoriamide adenine dinacleotide phosphate; NFIZ, nuclear factor (erythroid-derived 2)-like factor 2; UECD. Organization for isocomic Cooperation and Development; PSPS, phosphate buffered saline; H, propidium indder US6R, quantitative structure-activity relationship; REAH, Registration Evaluation Authorisation and Restriction of Chemicals; RIJ. relative luminescent unit; RP HPLC, reverse phase high performance liquid chromatography; RT, room temperature; 5DS, sodium dodecyl sulfate; T.C, treated cells: TNBS, 2.46-trinitrobenzene sulfonia acid.

Is; TNBS, 2,4,6-trinitrobenzene sulfonic acid.

Corresponding author. Fax: +49 211 2006 19209.

E-mail address: annette.mehling@basf.com (A. Mehling).

0273-2300/\$ - see front matter © 2012 Elsevier Inc. All rights reserved.

and xenobiotics. In particular, consumers and workers are often exposed to chemicals via cosmetic and household products or in industrial settings on a daily basis and to a significant degree. One of the adverse effects that can occur as a result of skin exposure to xenobiotics is contact sensitization, the clinical manifestation of which is allergic contact dermatitis (ACD). The principle objective of toxicological testing is to provide a basis for the assessment of hazards and to identify potential risks from use and handling of products, such as chemicals or cosmetic formulations, thus ensuring that adverse effects to human health do not occur. The evaluation of the sensitization potential of a substance has therefore been of central importance for hazard and risk assessments for decades. Currently, most toxicological endpoints in the regulatory context are assessed via animal testing. This is also the case for the sensitization potentials for which generally only the animal studies described in OECD 406 (guinea pig tests according to Buehler or Magnusson & Kligman) or OECD 429 and OECD 442 (murine local lymph node assays, LLNA) are accepted by the regulatory bodies.

The increasing emphasis on the ethics of animal testing has manifested itself in a regulatory context in the recent chemicals legislation on the registration evaluation authorization and restriction of chemicals (REACH (EU, 2006)) and even more so in

Compared to human		Accuracy
Animal test	Mouse LLNA	84%
Individual non- animal tests	DPRA	87%
	LuSens	82%
	MUSST	85%
	h-CLAT	78%
Combinations of non-animal tests (1 out of 2 is positive)	DPRA + LuSENS	85%
	DPRA + MUSST	81%
	DPRA + h-CLAT	83%
	LuSens + Musst	80%
	LuSens + h-CLAT	82%
Non-animal (2 out of 3) approach	DPRA + LuSens + MUSST	94%

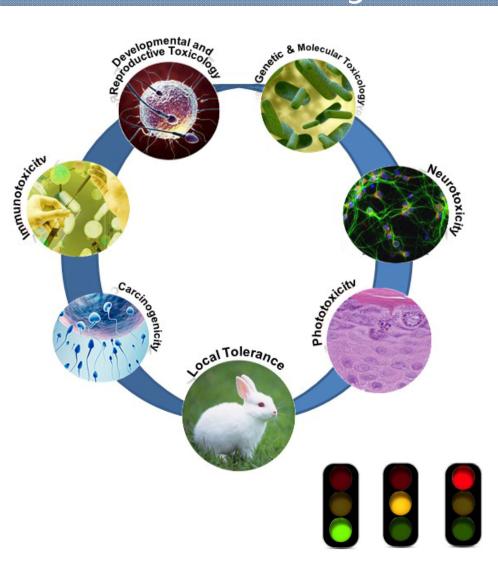
Non-animal replacement methods*

Health area	Test method (OECD guideline; year)	CONCEA	ANVISA
Skin corrosion	- Reconstructed human epithelium (TG 431; 2004) - CORROSITEX™ (TG 435; 2006)	2014 2014	2015 2015
Skin irritation	- Reconstructed human epithelium (TG 439; 2013)	2014	2015
Eye irritation	 BCOP (TG 437; 2013) ICE (TG 438; 2013) Fluorescein leakage (TG 460; 2014) Short time exposure (TG 491; 2015) EpiOcular™ (TG 492; 2015) 	2014 2014 2014 2016 2016	2015 2015 2015 - -
Skin allergy	- DPRA (TG 442C; 2015) - KeratinoSens (TG 442D; 2015) - h-CLAT (TG 442E; 2016)	2016 2016 -	- - -
Skin absorption	- Human post-surgical skin (TG 428; 2004)	2014	2015
Acute oral toxicity	- Starting dose guidance (GD 129; 2010)	2014	2015

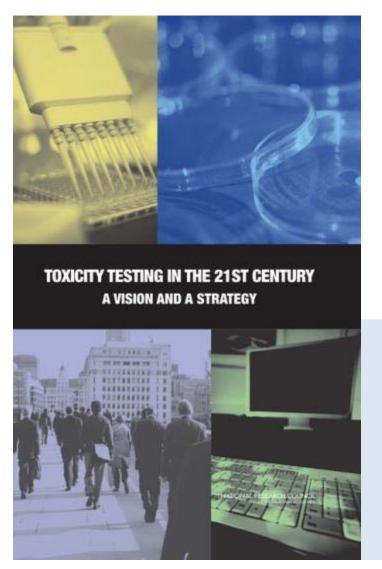
^{*} When used as part of an integrated approach to testing and assessment (IATA)

Replacement status of health areas relevant to cosmetic safety

- 1. Physico-chemical properties
- 2. Skin and eye irritation
- 3. Skin allergy
- 4. Photo-induced toxicity
- 5. Mutagenicity / genotoxicity
- 6. Acute toxicity (if oral $LD_{50} > 2000 \text{ mg/kg}$)
- Toxicokinetics (ADME)
- 8. Carcinogenicity
- 9. Repeated dose toxicity
- 10. Reproductive toxicity
- 11. Human data



U.S. National Academy of Sciences vision of '21st century toxicology'



"envisions a not-so-distant future in which virtually all routine toxicity testing would be conducted in human cells or cell lines *in vitro*"

"Animal testing won't disappear overnight, but the agencies' work signals the beginning of the end."

Elias Zerhouni, M.D.
Former Director
National Institutes of Health



Projected doubling in size of the in vitro testing market in 10 years

"The global *in vitro* toxicology testing market is expected to reach USD 27.36 billion by 2021 from USD 14.15 billion in 2016...

"Opposition to animal testing, new & promising technologies, increasing R&D to detect toxicity at early stages ... are the primary growth drivers."

http://military-technologies.net/2017/01/13/in-vitro-toxicology-testing-market-worth-27-36-billion-usd-by-2021/

Understanding the proposed bans

TESTING BAN

> SALES BAN

Testing ban needed to prevent new animal testing for cosmetic products and ingredients *in Brazil*

However, a test ban alone *cannot* prevent:

- New animal testing in Brazil claimed to be for 'non-cosmetic' purposes (e.g., chemicals)
- New cosmetic animal testing in other countries and import of these products or ingredients into Brazil

Sales ban needed to prevent cosmetic products or ingredients newly tested on animals in another part of the world from undermining Brazilian testing restrictions

Testing and sales bans support one another, ensuring equal treatment for domestic and foreign companies

Legislative history in Brazil

- Chamber Bill 6602/2013 by Deputy Ricardo Izar to modify Lei N° 11.794/2008 ('Arouca law') establishing procedures for the scientific use of animals; articles 14 (prohibitions), 17 and 18 (penalties)
- 2014 Bill moves to Senate; renumbered PLC Nº 70/2014*
- **2015-16** Report amending PLC N° 70/2014 prepared by Sen. Cristovam Buarque for Comissão de Ciência e Tecnologia (CCT) but never voted
 - **2017** Report amending PLC N° 70/2014 prepared by Sen. Randolfe Rodrigues and endorsed unanimously by CCT*
 - Bill moves to Senate Comissão de Meio Ambiente (CMA); rapporteur Sen. Jorge Vania

Official legal documents in Portuguese available online at:

- Lei Nº 11.794/2008: http://www.planalto.gov.br/ccivil 03/ ato2007-2010/2008/lei/l11794.htm
- PLC Nº 70/2014: https://legis.senado.leg.br/sdleg-getter/documento?dm=4768742&disposition=inline
- CCT report: https://legis.senado.leg.br/sdleg-getter/documento?dm=5130821

PLC N° 70/2014

Paragraph 7 The use any kind of animals in teaching, research and laboratory testing activities aimed at the development and production of cosmetics, personal care products and perfumes for ingredients with known effects and known to be safe for human use or for cosmetic finished products as defined by the regulation of the National Sanitary Surveillance Agency is forbidden.

CCT Amendments 2017

§ 11. The use of animals of any kind is prohibited in *tests* of personal hygiene *products*, cosmetics and perfumes, including tests aimed at evaluating their efficacy or safety.

--

This Law shall enter into force after three years from the date of its publication.

In relation to finished products, the prohibitions contained in this law are *effective immediately*.

TESTING BAN

PLC Nº 70/2014

TESTING

BAN

Paragraph 8 In the case of ingredients with unknown effects, the prohibition referred to in paragraph 7 will be applied in a period of up to 5 years following the recognition of alternative techniques capable of proving the safety for human use.

CCT Amendments 2017

§ 12. The use of animals of any kind in tests of ingredients that compose or may be made into personal hygiene products, cosmetics and perfumes, including tests intended to evaluate their efficacy or safety, shall be prohibited.

This Law shall enter into force after three years from the date of its publication.

The prohibition on the marketing of personal hygiene products, cosmetics and perfumes, as well as the ingredients that make them, that have been tested on animals do not affect the products and substances tested until the end of the period included in the caput.

PLC Nº 70/2014

No equivalent text

SALES BAN

CCT Amendments 2017

§ 13. The trade in personal hygiene products, cosmetics and perfumes, as well as their ingredients, which have been tested on animals, are prohibited.

--

This Law shall enter into force after three years from the date of its publication.

The prohibition on the marketing of personal hygiene products, cosmetics and perfumes, as well as the ingredients that make them, that have been tested on animals do not affect the products and substances tested until the end of the period included in the caput.

PLC Nº 70/2014

es 1

Paragraph 9 Internationally recognized alternative techniques will be accepted by the Brazilian authorities on a priority basis.

CCT Amendments 2017

§ 14. Internationally recognized alternative techniques will be accepted by the Brazilian authorities on a priority basis.



PLC Nº 70/2014

CCT Amendments 2017

DEROGATION

No equivalent text

- § 15. The national health regulatory authority, which is preceded by public consultation with civil society in exceptional circumstances, where serious concerns arise as to the safety of a cosmetic ingredient, may derogate from the prohibitions set out in the preceding paragraphs if the following conditions were simultaneously satisfied:
- a) it is an ingredient widely used on the market and can not be replaced by another capable of performing a similar function;
- b) To detect a *specific human health problem* related to the ingredient, in a reasoned manner;
- c) There is *no alternative method* capable of meeting the testing requirements.

Conclusions

- CONCEA has declared: "The tests are already carried out with alternative methods in Brazil and abroad. Therefore, the ban would not change the established scenario."
- More than 1,300 cosmetic companies (more than half the Brazilian beauty industry) are established in states where all cosmetic tests on animals are forbidden
 - ➤ No negative economic effect of bans reported in these states
- 37 national cosmetic animal testing/trade bans already in place and 10+ more under development
 - > Brazilian bans would help guard against future trade disruption with current and future export markets

Our ask

We urge the CMA to endorse all amendments to PLC No 70/2014 proposed by the CCT, without further changes

