

Ethics in cosmetic

PRODUCT

development ON

THE USE OF ANIMAL

AND HUMAN

SUBJECTS



COSMETI
Cs MUST
BE **SAFE**

- EU cosmetics directive

DO

OCCUR


SIDE EFFECTS



1000
participants

83 individuals
Complained of adverse reactions

10 INDIVIDUALS
Have allergic patch test reactions



DEBATE ON
COSMETIC SAFETY
AND ETHICS OF
TESTING IS NEEDED!

EU Council Directive 93/35/EEC

Regulates the
manufacture and
marketing of cosmetic
products in the EU



Safety Tests

- × Testing of finished cosmetic products is NOT required
 - × Testing of ingredients- EU or OECD- based
 - × Ingredient interaction

Tests to Support Claims

- × Documentation of claimed efficacy and support marketing

No “Cookery Book” Testing

A test method only gives answers related to the type of side effect it is developed for.

× Does it cause

- × **Acne?**
- × **Hair changes?**
- × **Skin irritation?**
- × **allergies?**

Symptoms are subjective

Reasoning and scientific background of the tests performed are needed



ANIMAL
TESTIN
G

Animal Testing

- × Animal tests → *routinely used* for skin testing of cosmetics
- × Proven *good predictivity* for significant skin sensitizers and corrosive and moderately irritant substances
- × However, the animal assays have *limited discriminative power*, when it comes to *mild effects*, as the ones expected from cosmetic ingredients and products
- × Animals are very different from humans
 - × Several structural and physiological differences
 - × Lacks the multitude of reaction patterns possible in human skin.

Animal Testing

- × Poor extrapolation: From animal-test data to human–consumer exposure risk
- × PETA
- × Because of these, animal testing was banned, and replaced with other methods
 - × Marketing after 2013 of cosmetics products which were tested on animals, as well as cosmetics with ingredients tested on animals, WHEN VALIDATED ALTERNATIVE TEST METHODS ARE AVAILABLE.
 - × Testing final products on animals.



HUMAN
SAFETY
TESTIN
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Ethical considerations

Finished cosmetics products must be shown to be essentially safe prior to human exposure

Transient effects are ethically acceptable

Adverse and permanent health effects are not

Ethical considerations

Clinical studies must add value to the understanding of the product toxicity and additional safety

To not generate a false-feel good factor which may be used for unethical marketing

Notes of guidance

At present, skin irritation human testing should not be preferred to animal testing

Irritancy reaction in humans is not an absolute measure

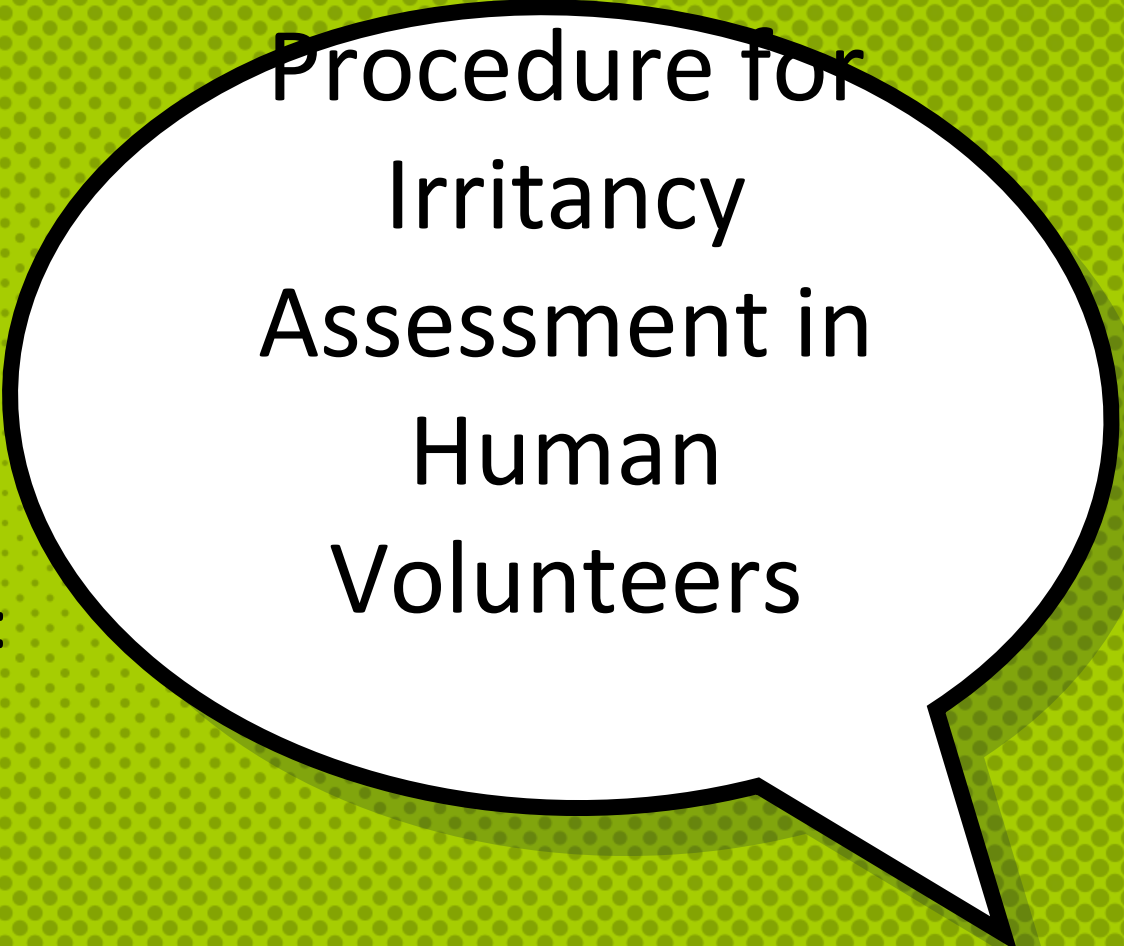
Scientific and ethical considerations need to be defined more clearly

Prerequisites for human testing

1. Tests in animals or validated alternative methods are of **limited value** regarding their predictive value for exposure of a human population. Therefore, **confirmatory safety tests in humans may be necessary** scientifically and ethically provided that the toxicological profile of a compound is available on the basis of animal or alternative methods.
2. Confirmatory testing of compounds in humans must only be undertaken when there is adequate information to suggest that a **high degree of safety is to be expected**.
3. Confirmatory tests of ingredients/products in humans must be limited to situations where **no irreversible damaging effects** are to be expected for the volunteers, and where the study goal is reasonably achievable with a study population of limited size.
4. **Human volunteers** should **not be employed** in investigation for **eye irritation** and **sensitization** or other toxicological trials where the outcome may be **irreversible**.

Prerequisites for human testing

5. The recruitment of human volunteers should be in line with the “World Medical Association Declaration of Helsinki” in its current revision: Human testing is to be conducted and monitored under the direction of relevantly trained personnel to ensure the health and well being of volunteer subjects involved in the testing. The **health and welfare of the subject has first priority and is highly protected.**
6. “The Good Clinical Practice for trials on Medicinal Products in the European Community” is a valuable guide.
7. National regulations regarding human studies should be followed.
8. Test protocols should be submitted to the responsible ethical committee.



Procedure for Irritancy Assessment in Human Volunteers

Available Protocols:

- × Open patch test
- × Closed patch test
- × Single exposure test
- × Repeated exposure test
- × Use test

Available protocols:

Open Patch Test

- × Applied to skin w/o occlusion (15 min -24 hrs)
- × Assessment of concentrated products

Close Patch Test

- × Occlusive chamber (24-28 hrs)
- × Comparative study of substances in same individuals


Available protocols:

Cumulative/Repetitive Closed Patch

- × Same test site (1-7x/wk for 1-5 wks)
- × Cumulative irritation

Used or Repeated Open Application Tests (ROAT)

- × Repeated application closely modeled to the use situation



Assessment of
Sensitization
Potential in
Humans

Human Sensitization

Tests:

- × Majorly conducted by contract laboratories
- × Vary in the number of induction patch tests, placing of patches, and use of a maximization step
- × Use of tests not entirely useful due to lack of validation

Approaches:

- × Single induction/single challenge patch test
- × Human Repeated Insult Patch Test
- × Human Maximization Test

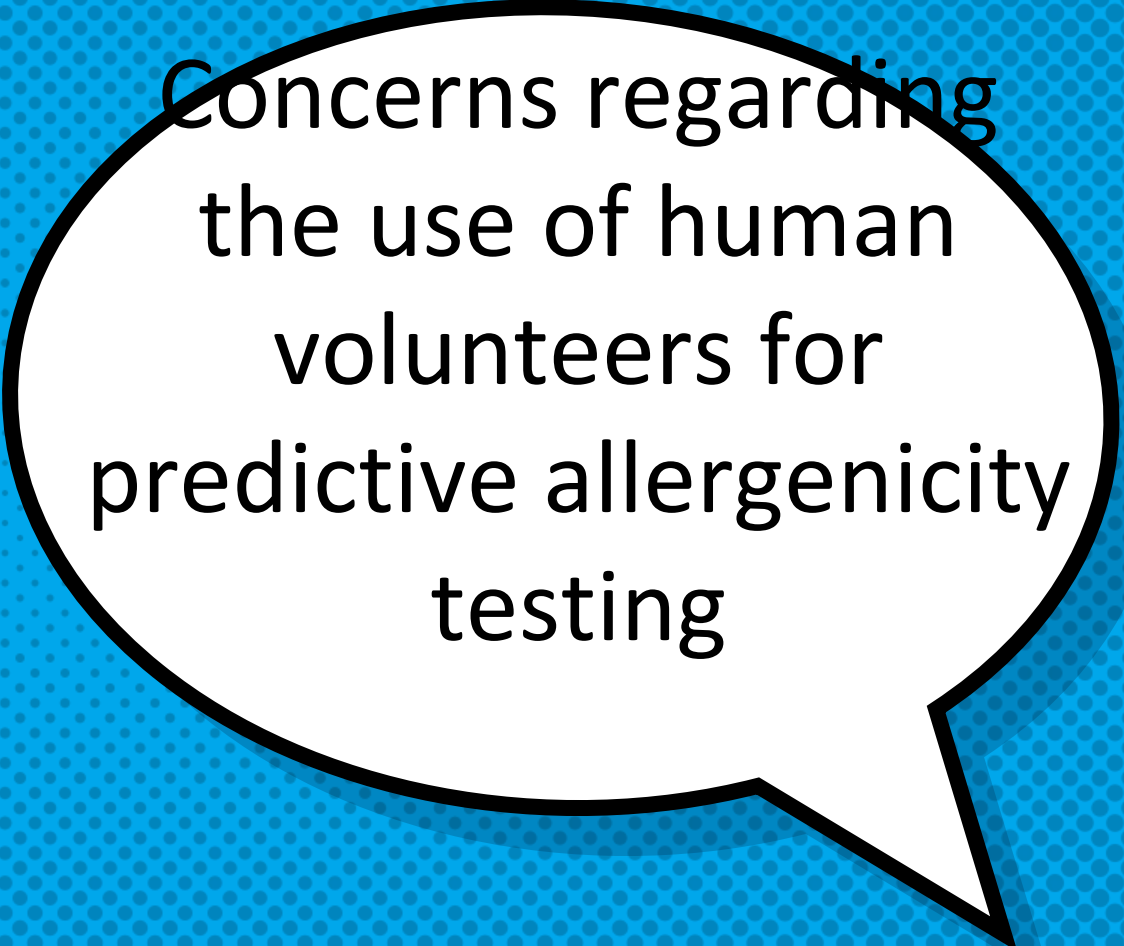
Test Performance

depends on:

- × Type of test substance
- × Chemistry
- × Toxicological data
- × Intended use of product



**DISCOURAGE
D!**



Concerns regarding
the use of human
volunteers for
predictive allergenicity
testing

SENSITIZATION TESTS

Sensitization test should always be done on animals

Because :


1. Time consuming
2. Very expensive due to large number of volunteers necessary
3. Often results to inhomogeneous test (compared to a more homogenous animal test)
4. Patch test sensitization may elicit clinical disease in the patient

Data in recent years:

2044 products tested on 136,765 person showed 123 cases of probable/confirmed sensitization

In conclusion:

Risk for human volunteers cannot be excluded because of lack of information on severity and frequency of adverse effect



Minimal
requirements for
human testing
for other
purposes

protocol!!!

Depends on:

1. Kind of cosmetic ingredients tested
2. Anticipated use of ingredient in the finished product
3. Kind of skin compatibility problem to be

Minimum requirement:

1. Positive control
2. Negative control
3. Scientific criteria for the chosen study design

THANK YOU!



PRESENTORS:

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