



COSMETICS EUROPE:
PRODUCT TEST GUIDELINES FOR THE ASSESSMENT OF
HUMAN SKIN COMPATIBILITY

1997

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1. BACKGROUND

The 6th Amendment to the Cosmetics Directive (93/35/EEC) includes a potential ban on the use of animals in the testing of cosmetic products and their ingredients from January 1, 1998.

With regard to assessment of skin irritation properties, the only test method approved by regulatory agencies (e.g. EU, USA) involves the use of rabbits in patch tests. This type of test is most useful for chemicals, (and is mandatory in the EU for new chemicals to assist in their classification), and finished products which are at the strongly irritant end of the irritancy spectrum. It is of little use for cosmetic products because the vast majority of such products have zero to mild irritancy.

For this reason, it is the considered opinion of most Colipa member companies that there is little point in developing a non-animal alternative to the rabbit skin irritation test for assessment of finished products.

Many Colipa member companies, in fact, assess not irritancy potential but skin compatibility of their products under controlled conditions in humans because the irritancy potential of most cosmetic products is very low. The great advantage of assessment in human skin is that extrapolation from rabbit to human is not necessary, and thus criticism of the relevance of effects in animals to potential effects in humans does not arise.

The members of the Colipa Human Skin Compatibility Task Force have many years of experience in the assessment of skin compatibility of cosmetic finished products in humans.

2. OBJECTIVE

The objective of this brochure is to outline the process and to develop guidelines for the assessment of skin compatibility of cosmetic products in humans.

Skin compatibility is defined as the absence of skin irritation under normal conditions of use and reasonably foreseeable misuse taking into account objective reactions as well as subjective responses such as stinging, burning or itching.

3. ETHICAL REQUIREMENTS

All human studies must be conducted in accordance with the Declaration of Helsinki (1964) and subsequent revisions (World Medical Association, 1989). They must be carried out by suitably trained, qualified and experienced personnel.

It is the responsibility of the investigator to take all precautions to avoid the possibility that participants in the study might experience undesirable effects. If any unusual risk to participants is involved the investigator should consider submitting plans for the study to an Ethical Review Committee. Such a Committee will review aspects of a study which may affect the safety and well-being of participants but responsibility for a study remains with the investigator (Schmitt 1994). Further suggestions of the ethical requirements which need to be taken into consideration in the planning of studies on humans are presented in Appendix 1.

4. TESTING APPROACH

In principle, the aim is to assess the compatibility of cosmetic products with the skin in studies carried out ethically on human volunteers. The goal can be achieved by using a cautious, step by step approach adapted to the product(s) to be tested. In some instances, the safety of the product under normal use conditions is assessed by testing under exaggerated use conditions. See, for example, Ippen 1986, Jenkins & Adams 1989, for tiered approaches to assessment of skin compatibility.

The following sections outline:

- the possible options available to assess the skin compatibility of cosmetic products;
- how to select the best approach for the type of product to be tested;
- the basic criteria for study initiation, conduct, and evaluation.

Whatever the method(s) used, the study must meet the requirements of responsible human testing which include the following issues :

- a safety assessment by a suitably qualified and experienced person is necessary for all products to be tested, e.g. to avoid the risk of inducing skin sensitisation;
- the planned study must satisfy ethical requirements;
- the objective of the study has to be well defined;
- the design of the study shall have sufficient power to be able to answer the question(s) set without imposing undue risk on the human volunteers;
- data management and data interpretation must be clearly defined;
- the sponsor and the investigator responsible for the conduct of the study must be clearly identified;
- a system for the management of adverse effects - should they occur during a study - must be established before the study begins.

5. PRE-REQUISITE INFORMATION ON TEST PRODUCT(S)

Before any human volunteers are exposed to test product(s), a safety assessment which includes considerations relating to toxicologically relevant issues is necessary (Scientific Committee on Cosmetology guidelines, 1990, see Appendix 2) . The safety assessment requires knowledge of the entire composition and stability of the test product(s). The trial can start only if the safety assessment concludes that no significant risk for the volunteers is to be expected under the conditions of the proposed study. The safety assessor may judge that it is necessary to obtain more data, (e.g. more precise specifications for raw materials, specific details of proposed exposure conditions) before completing the safety assessment.

6. GENERAL PROCEDURES

Since cosmetic products are expected to be of minor risk to human health due to their type, composition, mode of application and use, human testing can be performed directly after thorough safety assessment of the product(s) involved.

It is the general objective of skin compatibility testing to come as close as possible to the intended usage conditions, but under controlled test conditions.

The choice of test procedures depends on the type of product, its mode and frequency of use/application, the novelty of the ingredients, the risk for misuse of the product and the group of consumers expected to use it.

Since the most relevant information for safety and compatibility assessment is obtained from high numbers of actual exposures under intended use conditions, it is necessary to test representative groups of volunteers with adequate numbers of applications.

For some products, additional safety reassurance may be derived from tests using exaggerated but controlled exposure conditions (e.g. time, concentration). For screening purposes or comparison of product inherent properties, techniques involving standardised application which also exaggerate exposure compared to actual use can be considered (e.g. patch tests).

Whatever the product type to be tested and the procedures to be used, great care should be taken so that any reaction on human skin will remain very low. The objective is to assess the safety in use and/or foreseeable misuse but not to define the intrinsic irritant potential of the material to be tested. This objective will be achieved by a step by step approach.

In general, it is the responsibility of the individual(s) accountable for the safety assessment to decide whether or not human testing should be necessary and, with the investigator in charge of the conduct of the study, to develop a test study design which is appropriate to the problem in question.

Before any test commences, a general assessment of toxicological information for the ingredients of the products must be carried out and ethical implications of the proposed study must be considered.

Suggested test procedures to be considered for a significantly new formula without reference data from related products are:

- A : single application open epicutaneous test
- B : repeated application open epicutaneous test
- C : single application closed patch epicutaneous test under occlusion or semi-occlusion (exaggerated exposure compared to standard or reference product)
- D : repeated application closed patch epicutaneous test under occlusion or semi-occlusion (exaggerated exposure test to assess irritation thresholds or use limitations)
- E : controlled use test
- F : (uncontrolled) use test in the home

In the case of new formulations where data are available from use conditions or experimental application models with similar products, investigation of the new formula can start at the stage in the above procedure(s) at which comparison is appropriate.

In either case, test programmes can be terminated at the stage which has provided adequate information on the skin compatibility of the product under test.

For new formulations involving minor changes of composition which are not expected (in the experience of the experts responsible for the safety assessment) to influence skin compatibility, assessment of compatibility and release of product may be appropriate without any testing.

6.1 SPECIFIC REQUIREMENTS FOR DIFFERENT TYPES OF PRODUCT

Development of a test programme must take into account the type of application which affects the degree and duration of exposure for a consumer during normal use or a participant in the study of the product in question.

6.1.1 TYPES OF APPLICATION

A. RINSE-OFF PRODUCTS

Rinse-off products are normally considered to have only a transient effect on the skin, but it should be remembered that some chemicals can bind strongly to the stratum corneum even after a short contact time. Nevertheless, the result of a single application test or a short duration use test may be sufficient to reach a satisfactory risk assessment. However, in exposures involving repeated or frequent use (e.g. surfactant-containing products, use by professionals), the skin may not have sufficient recovery time between applications so that a cumulative effect may play a role. In such

cases, repeated exposure under use-related conditions is the only way to achieve an adequate assessment.

If prolonged or continuous or repeated contact is known to provoke a disturbance of skin function (e.g. barrier disruption by solvents, surfactants), comparative testing using patch test techniques (single or repeated application occlusive patch test) may be helpful in establishing the relative skin compatibility of the formula.

B. LEAVE-ON PRODUCTS

The ingredients in leave-on products of the skin care type, at the concentrations used in the products, are normally considered to be skin compatible. Patch testing of such skin care products generally reveals no adverse effects even after contact times of 24 hours. Nevertheless, experience shows that a product considered to be compatible after such a test procedure may, when applied to the face, provoke burning, tension or other sensations which cannot be assessed in a patch test procedure carried out on skin areas elsewhere on the body. Conversely, some active ingredients (e.g. moisturising agents, re- or de-fatting agents) in a formulation need some time of adaptation to reach a steady state of skin condition and product effect. Therefore, repeated and numerous applications under intended use conditions are necessary to assess the range of possible effects.

C. HAIR TREATMENT PRODUCTS

Permanent wave, reactive dye and similar products are not intended to be used on skin but often come into contact with it. Due to their irritation potential, the use of such products is mainly by hairdressers and only for careful use.

Due to their chemical nature and the fact that accidental contact with skin is foreseeable, such products require special consideration.

6.1.2 EXAMPLES OF TYPES OF TESTING ON HUMAN SKIN

See also Appendix 4 which gives details of the test methods and references.

Evaluation criteria are likely to be similar in all the following tests. Assessment is generally subjective, but may also be objective (Kajs and Gartstein, 1991, Serup and Jemec, 1995a) for example, transepidermal water loss (Nilsson, 1977, Pinnagoda et al., 1990) and redness intensity (e.g. Serup and Jemec, 1995b).

(a) Single application open epicutaneous test

This test is indicated in the case of novel formulations which are to be used for the first time on human skin and for formulations of high irritant potential, e.g. those manufactured for depilatory, hair waving, hair colouring, usage.

The test products are applied undiluted, usually to the arm, for exposure periods of up to 60 minutes. In the event of adverse effects, the tests can be stopped at any time.

Evaluations are performed visually, assessing, for example, redness, scaling, both during and following the exposure period.

(b) Repeated application open epicutaneous test

A decision whether to proceed with such a test or whether to proceed to patch testing will depend on the results of a single open application test.

The frequency of the repeat applications will be decided on a case-by-case basis.

A particular example of a test is the comparative assessment of surfactant-containing formulations and it is usually performed on an area of very sensitive skin.

Usually, a test formulation is applied to one elbow-flex (antecubital fossa) or forearm area and a reference formulation to the other elbow or forearm area of the same individual, under test conditions which are standardised with respect to exposure time, frequency, amount and concentration, solution temperature. The frequency of the repeat applications will be decided on a case-by-case basis.

Evaluations are made regularly, as specified in the test design, and may be both visual (scoring, e.g. redness, scaling) and objective (e.g. transepidermal water loss and redness intensity).

(c) Single application closed patch epicutaneous test under occlusion or semi-occlusion

This test may be used for new or novel formulations with known raw material, and for novel formulations which have been shown to be safe to skin in an open patch test. Comparative assessments of several formulations on the same individual, generally including one or more reference preparations, are feasible using this technique.

The test products are applied diluted or undiluted to the skin of, for example, the arm or back for periods of up to 48 hours under occlusive or semi-occlusive patches and evaluations are performed, for example, 1, 24 and 48 hours after removal of the patch.

The evaluation is performed visually, assessing, for example, redness, scaling, following the exposure period. Objective measurements of, for example, transepidermal water loss and redness intensity can also be made.

(d) Repeated application closed patch epicutaneous test under occlusion or semi-occlusion

This test may be used for the optimisation of formulations with regard to skin compatibility, especially for surfactant-containing products and for the evaluation of small differences between formulations of zero to mild irritancy which are used frequently and/or repeatedly, e.g. toilet soaps, hair and body shampoos. Reference products can be included in the tests.

For example, the preparations may be applied diluted on the forearm under occlusive or semi-occlusive patches, for example, 22 hours on the first day and 6 hours for each of the following 4 days (Frosch and Kligman, 1979).

In the event of strong reactions, the test can be stopped at any time.

The evaluations are performed each day after patch removal and before patch replacement, visually assessing, for example, redness, scaling. Objective measurements of, for example, transepidermal water loss and redness intensity can also be made.

(e) Controlled use test

This test may be performed under normal or slightly exaggerated use conditions but, in either case, the exposure/application conditions (which may vary widely for different product types) and evaluation are controlled and standardised.

(f) Use test in the home (uncontrolled)

This type of test is carried out on products under normal use conditions. The participants may be selected to represent different categories of consumer, e.g. of particular skin types.

Tests are performed using large groups of volunteers and over a test period of a duration which is considered to be adequate to evaluate skin compatibility under normal, uncontrolled, use conditions in the home, with periodic expert assessments of skin condition, and including comments by the volunteers on subjective effects. Such tests may also be useful in assessment of product efficacy and in establishing the acceptability of the product under test.

6.2 SUBJECT SELECTION

6.2.1 NUMBER

An adequate number of volunteers will be recruited to satisfy the objective of the test (both of which will be justified in the protocol) and the ethical requirements.

6.2.2 STUDY POPULATION

- Recruitment of volunteers/informed consent

Volunteers will be selected on the basis of inclusion and non-inclusion criteria. The volunteers must satisfy all the inclusion criteria and not conflict with any of the non-inclusion criteria. The volunteers must be clearly informed, verbally and in writing, regarding the nature of the study, the timetable, constraints and possible risks. They must then give their written informed consent before participation in the study is permitted.

- **Inclusion criteria**

- informed volunteers, where appropriate of relevant age, sex, ethnic origin, and health condition
- panellists will agree to follow the conditions specified in the Study Information Sheet (see Appendix 3)

- **Non-inclusion criteria**

- pregnancy or nursing condition (except where specifically required)
- blemishes, marks (e.g. tattoos, scars, sunburn) on the test site(s) which would interfere with scoring
- medication which may affect skin response or past medical history
- irritated skin on test site(s) (except where specifically required)
- any active skin disease which may interfere with the aim(s) of the study
- participation in another simultaneous study
- participation in a previous study without an appropriate rest period between studies

- **Withdrawal criteria**

Participants will be withdrawn if:

- they do not follow the conditions of the Study Information Sheet;
- they suffer any illness or accident or develop any condition during the study which could affect the outcome of the study;
- they no longer wish to participate in the study.

6.2.3 BALANCE OF GROUPS

Sex, age, ethnic origin, skin type of the volunteer panel should be selected in accordance with the appropriate user group of the product to be tested.

6.3 TEST MATERIAL(S)

6.3.1 REFERENCE MATERIALS

Reference materials should be used in each study in order to check inter- and intra-laboratory variations as well as inter-seasonal variability (e.g. Agner and Serup, 1989).

6.3.2 CONCENTRATION

The concentration of the product(s) will be adjusted according to the type of product, the test protocol and the objective of the study so as not to cause severe skin effects. Any dilution vehicle should be known not to cause adverse skin effects under the test conditions, otherwise it should be tested alone.

6.4 TEST METHOD

6.4.1 PRODUCT APPLICATION

Before the first product application or usage, participants will report to the test laboratory for expert evaluation, and, if appropriate, instrumental assessments, of skin condition.

Exposure conditions will be defined in the protocol, and will depend on the test type (see Section 6.1.2).

When appropriate, products will be randomised within and between subjects; skin areas with the highest likelihood of response variability (e.g. wrist, shoulder) should be avoided (Van der Valk and Maibach, 1989). In repeated patch studies, the patch site must be marked to ensure that successive patches are placed on exactly the same skin position.

See also Appendix 4 which gives details of the test methods and references.

6.4.2 DOSE LEVEL

In patch tests, the measured amount of test material applied to each patch must be sufficient to fill the chamber or saturate the pad without overflowing from it when applied to the skin. Solids should be moistened sufficiently with water to ensure good contact with the skin.

In use-related tests, the quantity of test material applied should be relevant to that expected to be used at home by the participant.

6.4.3 REMOVAL OF TEST MATERIAL

When appropriate, test product(s) will be removed in the laboratory by a technician. Test material(s) will be rinsed (or otherwise gently removed) from application sites without rubbing (to avoid cross-contamination).

6.4.4 EVALUATIONS

(a) Patch tests

Treatment sites will be assessed before the first application of test material (baseline), and after treatment at times defined in the protocol. In each case, there must be a specified period of time (e.g. 30 min) after patch removal before assessment.

Should any test sample elicit unacceptable responses it will not be reapplied on that participant for the remainder of the study.

(i) Visual assessment of skin compatibility

Reactions at the test sites should be scored throughout the test by the same experienced assessor who

made the baseline assessment and under the same lighting source, following a pre-defined scoring scale. An example of an established scoring scale is given in Appendix 5.

(ii) Instrumental measurements of skin compatibility

All instrumental evaluations will be made following an acclimatisation period in an environmentally conditioned room (e.g. below 22°C, constant relative humidity). Calibration of instruments will be checked regularly, and the instruments used as described in scientific literature or in the manufacturer's instructions. Such methods permit objective assessments and have been reviewed recently, (Kajs and Gartstein, 1991, Serup and Jemec, 1995 b).

(b) Use tests

Skin compatibility will be evaluated from:

- visual assessment of skin condition made at intervals during use of the product;
- a questionnaire to be completed by the participant.

(c) Statistical analysis

When relevant, the type(s) of statistical analysis (parametric, non-parametric) to be used must be valid and specified in the protocol which should also advise, in the case of repeated patch tests, on the handling of (lack of) data for sites which were not re-treated due to excessive response following the previous application.

(d) Data interpretation

Whilst this activity will always be on a case-by-case basis and will depend on the nature and type of study, the most common approach will be to compare the results from the new test product with those of positive and/or negative controls, or with similar products with a substantial history of safety in the market (which substantiates their skin compatibility).

7. STUDY REPORT

The final study report should include (but not be restricted to) information appropriate to the following headings.

(a) SUMMARY/ABSTRACT

Type and Objective of the study.

Number of participants and selection criteria for inclusion/non-inclusion.

Test materials and test procedures used.

Procedure(s) for assessment of effects.

(b) RESULTS

Number of participants starting and completing the study, including an explanation of any withdrawals during the study.

Presentation of data on test and reference materials used.

Presentation of subjective comments by participants.

Description (and justification, where appropriate) of any statistical procedures used.

(c) CONCLUSIONS/RECOMMENDATIONS

(d) APPENDICES

Copy of study protocol.

Identification of study investigators.

Copy of Study Information Sheet and written informed consent sheet.

8. REFERENCES

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APPENDIX 1

ETHICAL REQUIREMENTS

I All participants should be informed volunteers of relevant age, sex, ethnic origin, selected after application of inclusion/non-inclusion criteria (see Section 6.2.2).

II All participants must be made aware of the purpose and nature of the study and of any foreseeable risks involved in participation in the study and must give written informed consent before the test starts.

III Before any volunteers are exposed to the test material, all relevant safety information on the product and on its constituents must be evaluated.

IV All test procedures must conform to national regulations and, where appropriate, should be approved by an independent Ethical Review Committee.

V An Ethical Review Committee should include medical, non-medical, appropriate experts and lay members; it should consider the general ethics of the test and verify that the safety and integrity of the participants in the test are protected, taking into account information on the test material(s).

VI All reasonable care should be taken to avoid causing excessive skin reactions in the participants during a study.

VII Agreed procedures should be in place in the event of any unexpected/adverse reactions, including appropriate medical cover.

VIII Volunteers may be rewarded for their time, inconvenience, etc., but the reward must not be so great that it would persuade them to participate.

APPENDIX 2

EXTRACTS FROM THE SCIENTIFIC COMMITTEE OF COSMETOLOGY "NOTES OF GUIDANCE FOR TESTING OF COSMETIC INGREDIENTS FOR THEIR SAFETY EVALUATION".

Annex 2 of these notes of guidance notes states:

GENERAL TOXICOLOGICAL REQUIREMENTS FOR COSMETIC INGREDIENTS AND FINISHED PRODUCTS

A. When requested, the manufacturer shall provide the Commission with the information set out below.

1. Acute toxicity (oral or by inhalation in case of volatile substances);
2. Dermal absorption;
3. Dermal irritation;
4. Mucous membrane irritation;
5. Skin sensitisation;
6. Sub-chronic toxicity (oral or by inhalation in case of volatile substances);
7. Mutagenicity (bacterial test for gene mutations and in vitro mammalian cell culture test for chromosome aberrations);
8. Phototoxicity (in case of UV-light absorbing substances);
9. Human data (if available).

When considerable oral intake can be expected or when the data on dermal absorption do indicate a considerable penetration of the ingredients through the skin, taking into account the toxicological profile of the substance and its chemical structure, the following further information may be necessary:

10. Toxicokinetics;
11. Teratogenicity, Reproduction toxicity, Carcinogenesis and additional Genotoxicity.

B. Each cosmetic finished product is an individual and unique combination of ingredients.

“The dossier of a finished product or of a group of finished products should contain adequate information to make possible a safety evaluation of the finished product. In general, this would be obtained by a knowledge of the toxicity of the cosmetic ingredients. Toxicity information on the ingredients should include the evaluation of the most toxicologically-relevant end points.”

Reference

- Commission of the European Communities, Scientific Committee for Cosmetology. Notes of guidance for testing of cosmetic ingredients for their safety evaluation. First revision (CSC/803-5/90), approved by SCC during its 45th meeting (Oct. 2, 1990).

APPENDIX 3

EXAMPLE

INFORMED CONSENT FOR PARTICIPATION IN A STUDY

We are inviting you to take part in a test in which different test products, all of which are cosmetic products (e.g. soaps, shampoos, decorative cosmetics), will be placed on your skin. We will not specifically identify the test products to you. All the test products have been reviewed by a safety expert to ensure that the existing information on the products justifies human exposure.

Purpose and benefits

We wish to find out if any of the test products cause adverse effects on your skin. The results of the study will provide useful information for evaluating the safety of the products for their intended use. The tests will help in the development of products which can be used safely by millions of people.

Eligibility

If you would like to participate, we will first ask you to complete a questionnaire about your medical history, allergies, skin problems, any current medication and previous participation in similar skin tests. It is possible that, based on your answers to these questions, you may not be able to take part in the tests.

Test Procedure

All tests are conducted by experienced company employees.

[DESCRIPTION OF PARTICULAR TEST TO BE UNDERTAKEN]

Leaving the study

You are free to withdraw your consent and discontinue participation in the study at any time.

Risks and discomfort

You may experience some skin irritation during the course of the study, similar to a mild sunburn. The area of skin exposed to the product may become pink or red, and temporarily burn or itch or become dry. The most severe reaction anticipated would be redness, possibly, in the case of patch tests, accompanied by localised swelling. No permanent effects are anticipated.

EXAMPLE
CONSENT AGREEMENT

I hereby consent to take part in the experimental study which has been described to me and which will be supervised by [Dr/Mr/Ms.]. I understand that the study may involve some risk of adverse skin effects. This, and my part in the study, have been fully explained to me and I have had complete freedom to ask any questions about the study.

I understand that I am free to withdraw my consent to take part in the study and discontinue participation at any time. I also agree to inform the investigator of any changes in my health status or medication which might occur during the course of the study.

I will be able to ask for further information concerning the study, or report adverse effects, at any time by telephoning the investigator on [telephone number].

I agree that the data recorded during the study can be submitted to computerised treatment by the investigator, but understand that any information which can be identified with me will be kept confidential with the study records.

I have read and signed this consent statement with full knowledge of the facts.

.....
signature of volunteer

.....
printed name of volunteer

...../...../.....
date

APPENDIX 4

The references given demonstrate conditions, applications and examples of use of the techniques. Exposure times and concentrations are presented only as illustrations.

A. SINGLE APPLICATION OPEN EPICUTANEOUS TEST

Devices:	glass sticks, swab or cellulose paper
Test site:	inner forearm
Frequency of application:	once (for solid or cream leave-on products); for liquid products, repeated applications every 30 seconds may be made
Duration of treatment:	15 to 30 minutes
Removal of test substance:	by rinsing or gentle swabbing
Time(s) of assessment:	immediately record time when effect(s) first occur(s) immediately after last application, again after 24 & 48 hours
Parameters:	erythema, oedema, scaling adverse sensation(s) noted by participant
Grading:	zero, weak, moderate, strong
Evaluation:	number of subjects with effect(s) within defined time period, or occurrence of first response

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B. REPEATED APPLICATION OPEN EPICUTANEOUS TEST

Devices:	glass sticks, swab or cellulose paper
Test site:	elbow flex skin
Frequency of application:	twice per day
Amount of substance:	0.1ml
Duration of treatment:	one week
Removal of test substance:	by rinsing or gentle swabbing
Time(s) of assessment:	once per day before second application
Parameters:	rythema, oedema, scaling adverse sensation(s) noted by participant
Grading:	zero, weak, moderate, strong
Evaluation:	number of subjects with effect(s) within defined time period, or occurrence of first response; type of reaction

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C. SINGLE APPLICATION CLOSED PATCH EPICUTANEOUS TEST UNDER OCCLUSION OR SEMI-OCCLUSION

Devices:	OCCLUSIVE - large Finn Chambers, Hill Top or Leukotest (BDF) SEMI-OCCLUSIVE - Webril cotton and Blenderm tape
Test site:	upper arm or forearm
Frequency of application:	once
Amount of substance:	0.07 to 0.1ml
Duration of treatment:	24 hours (or any period from 30 minutes to 48 hours)
Removal of test substance:	by rinsing or gentle swabbing
Time(s) of assessment:	30 minutes after patch removal, then after 24 & 48 hours (72 hours)
Parameters:	erythema, oedema, scaling adverse sensation(s) noted by participant
Grading:	zero, weak, moderate, strong, very strong
Evaluation:	number of subjects with effect(s) within defined time period, or mean of score values after 3 readings, or area under curve for each parameter

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D. REPEATED APPLICATION CLOSED PATCH EPICUTANEOUS TEST UNDER OCCLUSION OR SEMI-OCCLUSION

Devices:	OCCLUSIVE - large Finn Chambers, Hill Top or Leukotest (BDF) SEMI-OCCLUSIVE - Webril cotton and Blenderm tape
Test site:	upper arm or forearm
Frequency of application:	once per day
Amount of substance:	0.1ml per application
Duration of treatment:	day 1: 24 hours day 2 - day 5: 6 hours each day
Removal of test substance:	by rinsing or gentle swabbing
Time of assessment:	on day 8
Parameters:	erythema, oedema, scaling, fissures adverse sensation(s) noted by participant
Grading:	zero, weak, moderate, strong, very strong for fissures only - zero, weak, moderate, strong
Evaluation:	mean of score values

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E. CONTROLLED USE TEST

Test type:	repeated open application under usage related conditions, but in the laboratory under supervision and, when appropriate, with reference materials. May also be used for studying effects of exaggerated usage conditions
Examples:	hand immersion tests, half-head test for skin care products or hair treatments
Devices:	depend on type of product and mode of application
Test site:	as intended in use
Frequency of application:	normally once or twice daily (if appropriate, even more frequently)
Amount of substance:	depends on type of product and mode of application
Duration of treatment:	1 to 3 weeks, depending on a steady state in biological response being reached (and the assumption that further use/exposure would cause no further increase in biological effects)
Parameters:	descriptive evaluation of objective and subjective parameters (e.g. erythema, chapping, discoloration, burning, stinging, etc.) comparison to effects of reference materials option to make instrumental readings (e.g. transepidermal water loss, spectroscopic measurements)

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F. (UNCONTROLLED) USE TEST IN THE HOME

Test type:	product usage under intended conditions, in the home
Number of participants:	50 or more
Selection of volunteers:	skin type, age, sex etc. according to intended user group (e.g. sensitive/aged/greasy skin etc) for test product
Test site:	as intended in use
Frequency of application:	as intended in use
Duration of treatment:	normally 4 to 6 weeks to ensure a sufficient number of exposures to product (times and frequency of use to be recorded by participant on diary sheet)
Parameters:	record of day of onset, duration, intensity of any responses, type of response; evaluation of number, duration and intensity of responses and types of response comparison to effects of known materials option to make objective instrumental readings

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APPENDIX 5

EXAMPLE OF SCORING SCALE

ERYTHEMA

- 0 = no evidence of erythema
- 0.5 = minimal or doubtful erythema
- 1 = slight redness, spotty and diffuse
- 2 = moderate, uniform redness
- 3 = strong uniform redness
- 4 = fiery redness

DRYNESS (SCALING)

- 0 = no evidence of scaling
- 0.5 = dry without scaling; appears smooth and taut
- 1 = fine/mild scaling
- 2 = moderate scaling
- 3 = severe scaling with large flakes

OEDEMA

- = absence of oedema
- + = presence of oedema

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Colipa, the European Cosmetic, Toiletry and Perfumery Association, was established in 1962. Its objectives are:

- ✧ To provide expertise and support to a range of working groups dealing in scientific, economic, fiscal, legal, consumer and environmental issues.
- ✧ To assist members in complying with European Union legislation affecting cosmetic industry products and operations.
- ✧ To act as an industry voice working with both international authorities and organisations. Additionally, Colipa provides a world-wide perspective to its members through its relationships with equivalent organisations in the USA and Japan.
- ✧ To serve as a communication and information centre for the European cosmetic industry, strengthening the industry's position through continuous interaction with its members.

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SCAAT has already taken a series of initiatives which will result in the execution of programmes and the generation of data to contribute to the validation of alternative methods. It is now recognised by the authorities as a credible and authoritative voice on this issue.

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