THE SCIENTIFIC COMMITTEE ON COSMETIC PRODUCTS AND NON-FOOD PRODUCTS INTENDED FOR CONSUMERS

OPINION

CONCERNING

BASIC CRITERIA OF THE PROTOCOLS FOR THE SKIN COMPATIBILITY TESTING OF POTENTIALLY CUTANEOUS IRRITANT COSMETIC INGREDIENTS OR MIXTURES OF INGREDIENTS ON HUMAN VOLUNTEERS

Adopted by the SCCNFP during the
plenary session of 8 December 1999

The SCCNFP has recently published guidelines on the use of human volunteers in the compatibility testing of cosmetic ingredients or mixtures of ingredients and on the use of human volunteers in the compatibility testing of finished cosmetic products. Compatibility testing in this respect is defined as the exclusion of irritation due to cosmetics and does not refer to the exclusion of sensitisation.

While these guidelines have given a more general perspective on the safety testing of cosmetics in human volunteers especially concerning ethical requirements, there is a need to specify basic criteria for study protocols of skin compatibility testing of potentially cutaneous irritant cosmetic ingredients or mixtures of ingredients on human volunteers.

These basic criteria will have to take into account :

- the mentioned SCCNFP guidelines:
  - Guidelines on the use of human volunteers in the testing of potentially cutaneous irritant cosmetic ingredients or mixtures of ingredients (SCCNFP/0003/98 Final)
  - Guidelines on the use of human volunteers in compatibility testing of finished cosmetic products (SCCNFP/0068/99 Final)

- the documents of referral cited in these guidelines :
  - World Medical Association declaration of Helsinki in its current revisions (1964-1975-1983-1989-1996)
  - Recommendation N° R(90)3, of the Committee of Ministries/Council of Europe adopted 4th February 1990
  - Draft directive on Good Clinical Practice for Trials on Medicinal Products in the European Community
  - National Regulations regarding human studies.

1- Study protocol

In all skin compatibility studies, a written study protocol is required. This protocol is to be submitted to an ethical committee provided that this committee conforms with the laws and regulations of the country in which the study is performed. On clearance by the ethical committee, the study is to be performed according to protocol unless amendments are authorised by the ethical committee.

The study protocol should contain information on the following :

- Name of the person responsible for the study
- Name of the study sponsor
- Study summary
- Scientific background
- Toxicological information on the ingredients or mixture of ingredients tested
- Purity of the ingredients
- Nature of the vehicle
- Aim of the study with a clear study hypothesis

- Design and methods of study
- Reporting of results
- Scientific literature

2- Study investigator

As stated in the previous SCCNFP guideline, skin compatibility testing involving human volunteers should be conducted only by technically qualified persons and under the supervision of a clinically competent medical doctor/physician. The physician in charge of the study has to be informed about the toxicological profile of the investigated cosmetic ingredients or mixtures of ingredients as laid down in the substance dossier.

3- Study aim and study hypothesis

One or more clear hypotheses should be stated in the study protocol. As a result of the study, these hypotheses will be refuted or accepted. Only a clear a priori statement of hypotheses will allow the choice of an appropriate study design, an appropriate study sample and choice of the appropriate statistical methods.

4- Study design

The design of skin compatibility studies depends on the study problem investigated. Many study designs have been described and successfully used in the past even though there are no protocols standardized and validated according to strict criteria. The study design will depend on :

- kind of cosmetic ingredient or mixture of ingredients tested,
- anticipated use of the ingredient or mixture of ingredients in cosmetic finished products,
- kind of skin compatibility problem to be assessed (e.g. sensory irritation, irritant dermatitis, acnegenicity), and
- acuity of skin compatibility problem to be assessed (i.e. immediate or delayed effects, acute or cumulative effects).

Typical study designs used successfully in the past for skin compatibility testing are the classic open and/or closed epicutaneous patch test for exclusion of acute irritant dermatitis, the 21 day cumulative patch test for the exclusion of cumulative irritant dermatitis and the facial stinging test for exclusion of sensory irritation.
All valid study designs for compatibility studies have to include negative and positive controls and the vehicle alone (blank).

The scientific criteria for the choice of the study design should be clearly stated in the protocol.

5- Study size

The necessary study size should be statistically based on the anticipated effect as described in the study hypothesis and on the type II error accepted for the study. For this purpose, a pilot study may be necessary. Skin compatibility studies without an adequate study size estimation have to be considered unethical.

6- Study participants

Inclusion and exclusion criteria for volunteers should be clearly described in the protocol. As stated in the previous SCCNFP guidelines, pregnant or lactating women and children should not be included in safety confirmatory tests except for specific exceptions. The same is true for volunteers with any current dermatitis or known past allergic contact dermatitis related to the ingredients or mixtures of ingredients tested.

7- Study treatments

The application of study substances should be clearly described regarding dose, time, and mode of application. It must be stated which substance is applied in which vehicle and galenic form. Application devices (e.g. type of chambers) should be specified in the protocol.

8- Study evaluations

The exact timing and mode of clinical evaluations of study participants should be described in the protocol.

Evaluation schemes (e.g. grading of skin reactions) and results interpretation criteria have to be detailed. Preference should be given to scoring systems that have found acceptance in the scientific community even though not formally validated (e.g. ICDRG scoring of patch test reactions).

If non-invasive skin bioengineering technology is used to assess skin reactions, the appropriate guidelines of the European Society of Contact Dermatitis (ESCD) or of the European Expert Group on Efficacy Measurements on Cosmetics and other Topical Products (EEMCO) should be followed (1-7).

9- Study data handling

Handling of study data should follow the requirements of Good Clinical Practice (GCP). In particular, all data entries and possible changes have to be documented to be traced back to time and responsible study investigator. All study documentation including all original study data forms have to be safely stored for a minimum period of 10 years. If study data are entered into information technology devices, the same criteria have to be fulfilled for safe data storage (8).

10- Statistical analysis

The statistical analysis to be used for the study data should be chosen and should be documented in the study protocol. Clear criteria for acceptance or dismissal of the study hypotheses should be given.

11- Study report

For each study, a final study report has to be written. Evaluation schemes and interpretation criteria have to be detailed. This report should contain a final statement on the acceptance of dismissal of the study hypotheses.

The ethical commission that has approved the study protocol has to be informed about unexpected side effects.

References

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