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Primary Irritation vs. Sensitization Test

Irritant Dermatitis: Skin irritation or irritant dermatitis results from direct damage to epidermal cells of the skin and have no immunologic component.

Primary Irritation (PI) or Cumulative Skin Irritation is used to determine the irritation potential of a test product. When exposure is sufficient and the offending agent is potent, classic symptoms of acute skin irritation are seen. The irritant reaction quickly peaks and is acute and then begins to heal upon removal of irritant. The onset is after one single exposure. The irritant reactions are the result of direct damage to epidermal cells of the skin and have no immunologic component.

The patches containing the test product are applied on the subjects' back and left for a period of 48 hours and test sites are evaluated approximately 30 minutes after removal.

Classification of Irritant Dermatitis:

Irritation	Patch Application (Exposure Period)	Evaluation	Onset
Acute (primary) irritant dermatitis	48 hour	Immediate upon removal	Acute, after single exposure
	4 hour or less	24 hour, 48 hour and 72 hour	Acute/delayed
Delayed acute irritant dermatitis	48 hour	12 hour and 24 hour	Delayed, 12-24h or longer
Cumulative irritant dermatitis	14 or 21 days	Immediate upon removal	Slowly developing (weeks), multiple exposures

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Contact Allergic Dermatitis: Skin sensitization or allergic contact dermatitis is a delayed immunologic response consisting of varying degrees of redness, irritation and itching which results from exposure of sensitized individuals to contact allergens.

HRIPT is a test for determining the **contact allergic dermatitis potential** of a test product. Allergic contact dermatitis/sensitization results when a substance contacting the skin has undergone an immunological alteration in its reactivity. This altered reactivity is the result of prior exposure material to the skin, which may lead to visual symptoms of erythema, edema, and papules. Unlike primary irritation, sensitization is a two-phase process involving totally distinct biological mechanisms. The first is the induction phase where the skin is initially exposed to the sensitizing drug. In the induction phase, the sensitizing drug or antigen is presented to the T-lymphocytes by the Langerhans cells of the epidermis. As a consequence, cells which recognize the antigen, proliferate and to some extent differentiate. The second subsequent phase, following the establishment of contact allergy, is elicitation where subsequent exposure to the sensitizing drug results in a manifested skin reaction. During elicitation, the antigen is once again presented mainly on Langerhans cells. The T-cells which have proliferated upon prior exposure now come to the treated site and initiate toxic events which result in local inflammation.

Methodology

- 50 subjects (100 or 200 subjects)
- 24h exposures for 3 weeks (alternate days) on upper/lower back
- 10-14 day rest period
- Single 24h exposure on naïve skin followed by evaluation at 24h and 72 h post-patch removal

Reference for PI: Weltfriend S, Ramon M, and Maibach H. Irritation Dermatitis, In Dermatotoxicology, 6th edition, CRC press, 2004, pp.181-235.
Reference for HRIPT: Weltfriend S, Ramon M, and Maibach H. Irritation Dermatitis, In Dermatotoxicology, 6th edition, CRC press, 2004, pp.235-262.

Please note that the references only provide details about the methodology and not claims for any of these studies.

The advantage of the PI test is that it can be completed faster than the HRIPT. However, it only provides irritation data and does not indicate if the product is allergenic (sensitizing). Only the HRIPT test can provide that data.

Why Perform the HRIPT test?
The testing is performed either for regulatory reasons or product liability reasons.

The Food and Drug Administration has authority over cosmetics sold in the United States. The section below is taken from the FDA web page cited below.

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Who is responsible for substantiating the safety of cosmetics?

Cosmetic firms are responsible for substantiating the safety of their products and ingredients before marketing. Failure to adequately substantiate the safety of a cosmetic product or its ingredients prior to marketing causes the product to be misbranded unless the following warning statement appears conspicuously on the principal display panel of the product's label:

"Warning--The safety of this product has not been determined." (21 CFR 740.10)

http://www.fda.gov/Cosmetics/GuidanceComplianceRegulatoryInformation/ucm074162.htm

However, the FDA does not specify which safety test needs to be performed. This decision is left up to each manufacturer. Personal Care manufacturers relies upon the industry guidelines created by the Personal Care Product Council (PCPC) – previously named Cosmetics, Toiletries and Fragrance Association. The recommendations are published in the "Safety Testing Guidelines". This guideline can be purchased from the PCPC organization. The general industry practice is to perform the 50 subject HRIPT as a minimum requirement for personal care products.

One other reason for safety testing is for product liability reasons. Many insurance companies require that some type of a safety test be performed prior to issuance of product liability insurance.

Another reason is to protect the brand name of the product or your company. Performing an HIRPT give you a minimum safety assurance that the formulation is generally safe for use on humans.

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What is meant by the Hypoallergenic claim?

Please see the attached link to the FDA website that describes the FDA position on hypoallergenic claim.
http://www.fda.gov/Cosmetics/CosmeticLabelingLabelClaims/LabelClaimsandExpirationDating/ucm2005203.htm

Hypoallergenic cosmetics are products that manufacturers claim produce fewer allergic reactions than other cosmetic products. Consumers with hypersensitive skin, and even those with "normal" skin, may be led to believe that these products will be gentler to their skin than non-hypoallergenic cosmetics.There are no Federal standards or definitions that govern the use of the term "hypoallergenic." The term means whatever a particular company wants it to mean.

Manufacturers of cosmetics labeled as hypoallergenic are not required to submit substantiation of their hypoallergenicity claims to FDA.The term "hypoallergenic" may have considerable market value in promoting cosmetic products to consumers on a retail basis, but dermatologists say it has very little meaning.

BioScreen's position on this claim is that it is up to the client to define it's meaning as stated by the FDA. We recommend 100 - 200 subjects be tested in an HRIPT with no reactions for the claim. This is the industry standard. However, since there is no accepted definition or government standard for the claim it is up to each individual client to determine what criteria they want to use to make the claim. BioScreen does not state on the reports that this claim has been supported.