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Tests on Cosmetics – Dreams and Realities

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Introduction

The cosmetic industry is booming and growing and so are the claims concerning the degree of amicability and effectiveness of cosmetic products. A cosmetic today has to fulfill many claims and demands and is not only due to the decorative effect. But, most over all, it has to be well-tolerated. But: not only the demands have changed, as well have the average skin-conditions. The skin conditions have gone to extremes in the population. There are growing groups with extremities in dry skin, sensitive skin and seborrhoic skin, that have to be considered in formulating, for problematic skin conditions work well and furthermore work well with cosmetic support.

Toxicity and Reglementation

Cosmetics are principally concerned with beautifying and decoration, rather than functionality. Formulation of cosmetics has been an exciting challenge for cosmetic chemists. Before formulating any cosmetic product, one must check the current regulations in the country where the proposed product will be sold to make sure all the effective components, vehicles and helping matters are going conform with those regulations. In the past, some matters had been used in cosmetics without any consideration for their possible toxicity. Today, all countries have regulations that control the type and purity of any materials that may be used in cosmetics. The active and passive ingredients are beforehand toxicologically attested harmless and appropriate.

The setting up of an appropriate vehicle requires not only a scrupulous selection of the raw materials, but also a deep knowledge of the remarkable problems linked to the difficulty of releasing several active principles at cutaneous level. Furthermore, it makes sense to use compositions, that are appropriate even for problematic skin conditions.

The European reglementations (76/768/EEC Council Directive and its Sixth Amendment (Council Directive 93/35/EEC)) require that a cosmetic product put on the market within the Community must not cause damage to human health and that the methods to replace animal testing must be scientifically validated as offering an equivalent level of protection for the consumers. The Inventory of chemicals commonly used since many years describing ingredients in cosmetic products includes some 8000 substances, and they belong to over 30 different usual cosmetic functions. The presence of chemicals potentially harmful to consumers' health among cosmetic ingredients is limited to a small number of substances, because the majority of raw materials employed in cosmetic products are recognized as harmless, on the basis of their widespread human use by consumers over many decades. It should be considered that the cosmetic industry has been a highly self-regulating body, providing quality products with remarkable absence of human toxicity. Out of the total number of cosmetic ingredients reported in the European Inventory, only 400 ca. (equivalent to 5%) are also separately listed in Annexes III, IV, VI, and VII of Council Directive 76/768/EEC as they were recognized since 1976 to represent some risk to consumers' health, and they were submitted to specific restrictions of use, after the evaluation of their potential toxic hazard towards consumers' health. The animal testing models for the safety evaluation of cosmetics and chemicals could not be replaced in the near future by a single *in-vitro* methodology. However, it is possible that, in a very short time for some of the tests (ocular and skin irritation, skin sensitization, phototoxicity, etc.), more than one method, including biological system(s) and intelligent systems(s), combined in a sequential could be defined and made available for distinct groups of chemicals (cosmetics). The possibility to further reduce the number of animals needed for the safety evaluation of cosmetic ingredients depends very much on the availability of reliable alternative methodologies which do not make use of animals. The most recent validation studies on a specific toxic endpoint, such as eye irritancy testing, has moreover demonstrated that one group of different methods (battery of tests) rather than one specific method is scientifically adequate to predict the potential for toxic effects of different chemicals.

The most important: Evaluating the allergic and sensitizing potential

After a cosmetic is assessed toxicologically and designed according to current regulations, dermatological tests have to be done to proof the dermatological amicability of certain substances. Amicability can

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be reduced mainly by Contact dermatitis and allergic dermatitis. The term contact dermatitis describes the inflammatory condition of the skin caused by external agents and is most often seen on skin sites frequently exposed to cosmetics (face, hands). The clinical appearance is extremely variable. Contact dermatitis is produced by irritant substances or by allergic mechanism, some times strengthened by UV radiation. Irritant contact dermatitis is a mechanism where a substance damages the skin barrier and produces cell damage. Allergic contact dermatitis does not occur in every individual, sensitization has to occur before.

The risk of sensitization depends on individual susceptibility and is genetically determined, for siblings and children of patients suffering from allergic contact dermatitis have an increased incidence of positive patch testing. Local factors are important for the development of allergic skin disease. Sensitivity is most easily acquired if the allergen is applied to damaged skin. To provoke an allergy, an artificial skin damage is produced by previous application of sodium lauryl sulfate.

The sensitizing properties of the substance applied often depends on its concentration per square unit of the skin. With high concentrations of a strong allergen (such a DCNB), the individual susceptibility is of little importance; nearly everyone is capable of being sensitized.

With most substances encountered in daily life sensitization occur only in exceptional cases, commonly after prolonged contact. Th time between first contact and the onset of the sensitization depend partly on the sensitizer and the conditions of exposure, partly on cor stitutional factors and partly on coincidental lowering of the resis tance of the skin favouring the development of dermatitis.

The sensitizing processes are complete within 5 days. Reaction: between the antibody-like substances formed and the allerger remaining in the skin need a further 24-48 hours to develop. If the sensitized person is re-exposed to the specific allergen in sufficien concentration a clinical reaction develops usually between 24 and 48 hours later.

This fact is made useful for the discovering of allergens. The patch test is performed with the possible allergy-causing substances. For this, all the substances, or the whole cosmetic or other agent thought to be an allergen is applied with patches to the healthy skin of the upper arm or the back of the patient and occlusively left there for 24-48 hours, possible reactions are examined after 48 and 72 hours. Once acquired, contact sensitivity tends to persist. The degree of sensitivity may decline unless boosted by repeated exposures, but with a high initial level of sensitivity it usually remains demonstrable throughout life.

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Supporting of claims on cosmetics

A cosmetic claim is a benefit that can be perceived by a consumer when using either a decorative cosmetic or a skin care product. The legal classification of what cosmetics are and regulatory systems vary in the different parts of the world. Regardless, cosmetic claims must be substantiated which means that they must have what is called a reasonable basis to support the cosmetic's claim.

There are three ways to substantiate a cosmetic claim:

(1) by testing the cosmetic to demonstrate that customers experience supports the claim

(2) by expert analysis and opinion which typically involves a review of already published information on a cosmetic ingredient or product type.

(3) by specified test methods that support the claims to be made

To find out the consumers' opinions about and new demands concerning a product, dermatological in-use testing is an often used and proved method. In-use tests with subsequent patch-testing for exclusion of a high certainty of sensitization is often combined with a questionnaire or discussion groups or test methods to prove the effectiveness of a single cosmetic. In some cases a co-operation with adjacent to dermatology, such as odontology, ophthalmology and gynaecology is necessary. The in-use test lets the consumer come in intensive contact with the product and so she or he can judge about the positive and eventual negative properties of the tested product. Within this long period of usage, the consumer can judge about the application method, the promised effect and its duration.

Careful selection of volunteers

These test-procedures can be applied on all groups of probands and the collective of probands can be chosen arbitrarily and fitting to the belongings of the producer and the target-group and may even include babies or toddlers in the in-use group, to prove the amicability to sensitive skin. An subsequent patch-testing can not be done on the baby-group for ethical reasons, and has to be done on a group of adults with sensitive skin.

The most important volunteer groups with sensitive/problematic skin conditions are:

- Defined sensitive skin panels: Fragrances, Nickel, Preservatives
- Pathological condition panels: Atopics, Acne, Psoriatics, Diabetics
- Ethnic panels
- Chronological panels: New-born, Elderly
- Treatment/medicated panels: Vitamin A, AHAs
- Environmentally stressed panels: low humidity/low temperature-sun exposed
- Occupational panels: Frequent hand washing/Solvent exposed

In the past, panellists with normal skin were used for dermatological testing. Testing on individuals with sensitive skin was thought to yield results that were uninterpretable. For more than 10 years individuals with sensitive skin began to be used in testing. The reason sensitive skin panels have now been used is twofold. First, our scientific and clinical knowledge of what sensitive skin is with its various subsets, has increased dramatically. Second, consumer surveys since the 1990s demonstrate that between 50 and 70% of consumers perceive their skin to be sensitive. In the 1980s, only 25-33% of all consumers perceived their skin to be sensitive. Therefore, substantiating a cosmetic claim in panellists who have defined sensitive skin can provide a strong support for various cosmetic claims.

Experienced dermatological and medical control and advice is needed

The most challenging tasks in supporting a claim is providing credible supporting data. One must understand the anatomy and physiology of the skin and the tools available to measure product effects at the level they are occurring. Moreover, it is important to leverage information directly extracted from the panelist's experience while using the product. Lastly, one must choose the best method of analysis and presentation of the data to draw conclusions that provide credible substantiation of a product claim.

The success of a clinical trial is dependent upon the recruitment of qualified subjects that are appropriate for the design and the purpose of the study. Examples of criteria that need to be considered include age range of the panel, gender, and whether a certain skin profile is required. Furthermore, clinical assessment involves careful inspection of the skin, usually under magnification and blue daylight lightening by a dermatologist trained to grade the full range of a skin attribute. Clinical grading can be particularly beneficial for assessing skin attributes that are not easily measured with bioinstrumentation. Other more subtle, but important considerations for eligibility criteria are e. g. excluding individuals who have a recent history of using other similar preparations, and excluding individuals with medications that may interact with the active ingredients or may mask adverse reactions resulting from test product usage such as anti-inflammatory drugs, or medications that provoke hypersensitive to sunlight.

Modern Cosmetics today are getting more and more compatible and efficient over the last years. This is with highest certanity due to scientifically based and validated medical research and co-operation of scientific research and producers.

(References can be ordered at the authors', please contact us at www.dermatest.de)

化妆品试验 – 梦想与现实

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导言

化妆品行业繁荣兴旺、发展迅速，而有关化妆品的亲和度与效力的声言也不甘其后。今天的化妆品要满足许多声言和需求的要求，而不只是达到装饰性效果。然而，最重要的是，它必须有很好的耐受性。但是，不仅需求发生了变化，一般皮肤条件也发生了变化。人们的皮肤条件已经走向极端。具有极端干燥，过敏型和油腻皮肤的人越来越多。配方中需要考虑到这个问题，以便解决问题皮肤的问题，并使它们能够更好地得到化妆品的支持。

毒性与管理规定

化妆品的主要关切是美容与装饰，而不是功能方面的问题。化妆品的配方一直是化妆品调剂师面临的激动人心的挑战。在调配任何化妆品之前，都必须查看将销售有关化妆品的国家的现实法规，以确保所有有效成份、载体和辅助成分都能符合这些法规。过去，有些化妆品使用的成份根本没有考虑到它们可能具有的毒性。现在，所有国家都制定了相关法规，以控制化妆品可能使用的材料的类型和纯度。活性与非活性成分都在事先进行了毒性测试，以确保它们是无害的和适宜的。

建立一种载体不但需要谨慎选择原材料，还需要深入了解与皮肤表面释放若干活性要素的困难有关的特殊问题。另外，有理由使用甚至适宜问题皮肤条件的合成物。欧洲的管理规定（《理事会指令》76/768/EEC 及其第六次修正案（《理事会指令》93/35/EEC））要求，进入欧盟市场的化妆品不能损害人类健康，取代动物试验的方法必须是经过科学验证的，从而能够为消费者提供相同程度的保护。多年来常用的描述化妆品成份的化学品清单包括大约 8000 种物质，它们具有 30 多种不同的一般化妆品功能。化妆品成份中只有极少数物质对消费者的健康构成潜在危害，因为消费者数十年的广泛使用结果证明，化妆品中使用的大多数材料都是无害的。应该把消费品行业看作高度自律的行业，它提供对人类显然无害的高质量产品。在《欧洲目录》中所包括的全部化妆品成份中，只有大约 400 种（相当于 5%）成份被分别列入了《理事会指令》（76/768/EEC）的附录三、附录四、附录六和附录七。因为自 1976 以来，人们已经认识到它们对消费者的健康构成一定风险，并在评估了这些物质对消费者健康的潜在危害之后，具体限制了它们的用途。在近期内，还不能用单一的体内方法取代评估化妆品和化学品安全所需要的动物实验模式。然而，对有些试验来说（眼睛与皮肤刺激、皮肤致敏、光毒性，等等），可能在很短的时间内就可以确定按顺序组合的多元方法（包括生物系统和智能系统），以测试不同类型的化学制品（化妆品）。进一步减少化妆品安全评估所需要的动物数量在很大程度上取决于是否能够找到不使用动物的其它可靠方法。另外，最近对一种具体毒性终端进行的验证研究（如眼睛刺激试验）表明，用一组不同的方法（试验组）而不是一个独立的方法预测不同化学品的潜在毒性作用是很科学的。

最重要的工作：评估过敏与致敏潜力

当一种化妆品经过毒性评估并按照当前管理规定的要求设计之后，必须完成皮肤试验，以证明具体物质的皮肤亲和

性。接触性皮炎和过敏性皮炎会降低亲和性。接触性皮炎一词指的是由外部因素引起的皮肤炎症，往往发生在经常使用化妆品的皮肤部位（脸、手），临床外貌差异很大。接触性皮炎是由刺激性物质或过敏性机制引起的，有时紫外线辐射会起到恶化作用。刺激型接触性皮炎是这样一种机制，其中一种物质破坏了皮肤屏障，造成了细胞损害。不是所有的人都会得过敏型接触性皮炎，此前必有致敏作用。

致敏风险取决于个人的敏感程度，后者是由遗传因素决定的，因为患有过敏型接触性皮炎的病人的兄弟姐妹和子女在接触性试验中结果呈阳性的概率越来越高。局部因素对过敏型皮肤病的发生也有重要影响。如果把过敏原放到受损伤的皮肤上，就很容易产生过敏反应。可以通过先前使用十二基硫酸钠造成的皮肤损害产生过敏反应。

应用物质中的致敏属性往往取决于其在单位面积皮肤上的浓度。在一种过敏原（如 DCNB）浓度很高的情况下，个人的敏感程度就没有什么重要意义了；几乎所有的人都有可能被致敏。

人们在日常生活中接触到许多物质，但致敏情况只是特殊的例外，往往发生在长期接触之后。从第一次接触到开始过敏，这段时间的长短部分取决于过敏原和风险条件，部分取决于体质因素，部分取决于同时降低的皮肤抵抗皮炎的能力。

致敏过程在五天之内完成。已经形成的抗体物质和停留在皮肤上的过敏原还需要另外 24 至 48 小时才能逐步发生交互反应。如果被致敏的人重新回到具体过敏原达到充分浓度的环境中，一般会在 24 至 48 小时之后发生临床反应。

人们通过这个事实来发现过敏原。皮肤过敏试验使用了可能的致敏物质。为了进行这种试验，人们把所有物质，或所有化妆品或其它他们认为可能是过敏原的载体，都贴到病人上臂或背部的健康皮肤上，让它们在那里停留 24 至 48 小时，并在 48 至 72 小时之后观察可能发生的反应。

一个人一旦产生过敏反应，接触性过敏一般就会永久存在。除非反复接触提高了过敏程度，过敏程度有可能下降；但如果原本过敏程度就很高的话，往往一生都会表现出来。

支持化妆品的声言

化妆品声言是消费者在使用装饰型化妆品或护肤型产品时可以感觉到的效益。世界上不同地区实行不同的化妆品法律分类和管理体制。尽管如此，化妆品声言必须得到证实，即它们必须具有能够支持化妆品声言的合理基础。

有三种证实化妆品声言的方法：

(1) 通过测试化妆品来表明消费者的体验支持有关的声言；

(2) 通过专家分析和意见支持有关的声言，这种分析和意见一般涉及对已发表的有关化妆品成份或产品类型的信息的回顾；以及

(3) 通过指定的试验方法来支持已经作出的声言。

要了解消费者对某种产品的看法和对某种产品的新需求，皮肤应用试验是经常使用并屡试不爽的方法。在排除致敏作用确切性的皮肤过敏试验之前进行的应用试验往往还同时使用以下方法来确定某种产品的效力，即问卷调查或讨论小组或试验方法。在某些情况下，还有必要与皮肤科相邻的学科进行合作，如牙科、眼科和妇科。应用试验使消费者与产品密切接触，因此使她或他能够判断试验产品的正面与最终的负面属性。在

长期的使用过程中，消费者可以对产品的使用方法、承诺效果和期限作出判断。

谨慎选择自愿者

为了证明产品对过敏性皮肤的亲和力，这些试验程序可以用于所有的试验小组；可以任意选择试验者群体，其中包括生产者和目标群体的眷属；甚至可以在应用试验小组中包括婴幼儿。由于伦理方面的原因，随后的皮肤过敏性试验不能在婴儿组进行，只能在过敏型皮肤的成年人群体中进行。

最重要的皮肤过敏型/问题型自愿者群体是：

- 确定的过敏型皮肤试验小组：香料、镍、防腐剂
- 病理条件试验小组：特异反应、痤疮、牛皮癣、糖尿病
- 按种族划分的试验小组
- 按年龄划分的试验小组：新生儿、老年人
- 治疗/药疗试验小组：维生素 A、果酸
- 受环境影响的试验小组：低湿度/低温度/暴露在阳光下
- 职业试验小组：频繁洗手/受溶剂影响

过去，人们用正常皮肤的试验小组成员做皮肤试验。他们认为用过敏型皮肤的人做试验会得出无法解释的结果。十多年以前，人们开始用过敏型皮肤的人做试验。使用过敏型皮肤试验小组有两个原因。第一，我们对过敏型皮肤及其各种亚群体的科学和临床知识显著增加了。第二，1990 年代以来的消费者调查表明，50%至 70%的消费者感到他们的皮肤是过敏型的。在 1980 年代，在所有的消费者中，只有 25%至 33%的人感到他们的皮肤是过敏型的。因此，在具有确定的过敏型皮肤的小组中证实消费者的声言可以为各种化妆品声言提供有力的支持。

经验丰富的皮肤和药物控制与建议是必要的

支持一项声言的最大挑战是提供可信的支持数据。必须了解皮肤的解剖学和生理学以及可以在产品产生效果的层面上衡量产品效果的工具。另外，重要的是在使用产品的同时，正确利用从试验者的经历中得出的直接信息。最后，必须选择最佳的分析方法和数据展示方法，以便提炼出能够可靠地证实产品声言的结论。

临床试验的成功取决于聘用符合研究的设计和目的的合格的试验者。必需考虑的标准包括试验小组的年龄范围、性别、以及是否需要某种具体的皮肤类型。另外，临床评估包括仔细观察皮肤，一般要由一位受过培训、能够评定各种皮肤特征全部内涵的皮肤科医生通过放大镜和蓝色自然光照来完成。在评估不易用生物仪器衡量的皮肤特征时，临床评定尤其有益。在资格标准方面，其它较微妙但很重要的考虑是，排除那些最近使用过其它类似制剂的个人，并排除那些使用了以下药物的个人，即可能会与活性添加成分发生相互作用的药物，或可能会掩盖使用试验产品产生的负面反应的药物，如抗炎药、或造成对光线严重过敏的药物。

与前几年相比，当代化妆品目前的兼容性和效率越来越高。这是建立在科学基础上的和经验证的医学研究以及科学研究和生产者的合作产生的最毋庸置疑的事实。

（可以向作者索取参考目录。请通过以下网址联系我们：www.dermatest.de）