CODEX
BEAUTY LABS

Chapter: Product Safety Testing

SECTIONS

01 Should I care about safety?

When it comes to skincare products, consumers invariably focus on product performance. They select products based on the performance claims used to market the product, hoping they are accurate and as represented, while taking product safety for granted. While there is certainly no denying the importance of product performance, application of an unsafe product onto one's skin, regardless of how well it performs, is never an acceptable trade-off. That is why reputable companies who care about the image and reputation of their brands, and of course the health and well-being of their consumers, engage in rigorous safety testing prior to releasing their products to the public.

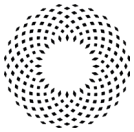
02 The four pillars of product safety: ingredients; manufacturing; stability; and allergy testing.

INGREDIENTS

When it comes to ingredient safety, most people are quite surprised to find out that the European Union has banned the use of more than 1,000 ingredients in cosmetic products, whereas the FDA has identified a mere 11 banned ingredients. On the surface, it appears as though the regulatory bodies in the EU take the safety of the ingredients applied onto their citizens' skin a bit more seriously than their US counterparts. Change, however, is at least once again on the congressional table with the proposed Cosmetics Safety Enhancement Act. It's been more than 80 years since a House committee has voted to make health and safety reforms in the cosmetic industry. This bill, if passed, would require companies to test the safety of their products and notify the FDA of any health concerns. In the meantime, consumers are forced to either not think about what's in their products or assume that their chosen brand has performed a reasonable level of due diligence regarding the safety of the ingredients contained in their products.

Although there is currently no governmental agency responsible for vetting the safety of cosmetic ingredients, there are non-governmental organizations (NGOs) that have taken on that responsibility for the time being. One such organization is the Environmental Working Group (EWG). They are a non-profit that serves as a sort of watchdog for the cosmetic industry, attempting to educate consumers on which ingredients present in products should be avoided. To that end, they have created a database of ingredients called Skin Deep which contains a list of ingredients found in over 41,000 products that are cross-referenced with 50 third-party toxicity and regulatory databases in order to enable consumers to make their own informed decisions as to which ingredients/products should be avoided.

Yet another cosmetic industry watchdog group attempting to keep consumers informed as to the safety of the ingredients in their products is the Campaign for Safe Cosmetics. Their mission is to secure the corporate, regulatory and legislative reforms necessary for keeping ingredients characterized as being dangerous out of cosmetic and personal care products. While the existence of such groups is certainly beneficial from an information gathering and communication perspective, the ultimate burden falls on cosmetic companies themselves to perform the level of due diligence necessary for them to be confident that the ingredients in the products are safe. This is done by vetting the suppliers of cosmetic ingredients to ensure that they have properly tested their ingredients for safety and can provide the documentation and certifications necessary to quantitatively substantiate their findings.



MANUFACTURING

The second pillar of product safety relates to how the products are manufactured or, more particularly, the processes, procedures and environment in which they are made. Those companies that place a high level of importance on safety when it comes to product manufacturing are most likely to adhere to guidelines created by the International Organization for Standardization (ISO). ISO 22716:2007 sets out guidelines for the production, control, storage and shipment of cosmetic products. These international guidelines are intended to communicate best manufacturing processes to the global cosmetic industry.

Similarly, in the United States, while the Food and Drug Administration (FDA) does not currently regulate cosmetics, the Federal Food, Drug and Cosmetic Act prohibits the introduction or delivery, in interstate commerce, of cosmetics that are adulterated or misbranded. Cosmetics are deemed to be "adulterated" if the product: (1) contains a potentially harmful substance; (2) contains filth; (3) contains a non-permitted/non-certified color additive; or (4) has been manufactured or stored under insanitary conditions. This law facilitates the entering and inspection of the manufacturing establishments themselves, including their equipment, finished and unfinished materials, containers and labels. In general, the act's guidelines for good manufacturing practice (GMP) call for a vetting of a manufacturer's:

- Building and facilities to make sure they are sanitary and in good working order
- Equipment to ensure it is appropriately designed and maintained
- Personnel to make sure they have been properly trained to perform their function in a clean and safe manner
- Raw materials (ingredients) to ensure they are properly stored, handled and tested for contamination
- Production processes and procedures with regards to formulation, processing, transfer/filling and in-process control methods
- Laboratory controls pertaining to raw materials/samples/finished product testing for contaminants
- Records maintenance and retention policies to ensure that all of the documentation necessary to substantiate the processes, procedures and safety of the manufacturing process are being strictly adhered to
- Labeling to determine whether the information on the packaging is comprehensive (e.g., states instructions for use/listing of ingredients), correct and contains all of the necessary warnings

PRODUCT STABILITY TESTING

The third pillar of product safety relates to stability, i.e., the inhibition of premature degradation caused by unwanted chemical reactions involving a product's ingredients and microorganisms present in the product. Beauty products are typically formulated to be stable over a period of 1-3 years from their date of manufacture and/or 1-2+ years from their date of first use. Cosmetic products, like virtually all products, have a limited shelf life and will naturally degrade over time. It is thus critically important to perform stability testing on a product prior to releasing it to the public in order to ensure that it will remain safe to use during its shelf life.

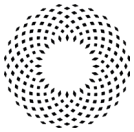
In general, stability testing of cosmetics generally encompasses evaluating three categories of product stability: microbiological stability, physical/chemical stability and packaging stability. It is not until a product achieves satisfactory results in all three of these categories that it can be considered safe to use over the course of its intended shelf life. ISO has created standards for stability testing: ISO/TR 18811:2018(en) Cosmetics — Guidelines on the stability testing of cosmetic products [4].

ALLERGY TESTING

Cosmetic products can provoke allergic reactions in some people (many people suffer from allergies and anyone at any age can develop allergies). Even substances may be harmless, when you immune system overreacts to them, you can have an allergic reaction. Allergens trigger the immune system to release antibodies that result in allergy symptoms, such congestion caused by pollen from blooming plants, or anaphylaxis from a peanut food allergy. Cosmetic allergic reactions most often appear as itchy, red rashes on the skin, called contact dermatitis.

The best way to prevent an allergic reaction from cosmetics or skincare is to know what you are sensitive to and simply avoid it by carefully reading the product ingredient panel. Unfortunately, it isn't enough to check for terms like "hypoallergenic", "fragrance-free" or "for sensitive skin," as there is no FDA standards or definitions that govern the use of these terms in the U.S. and these terms are now illegal to use in Europe. However, under the authority of the Fair Packaging and Labeling Act (FPLA), the U.S. Food and Drug Administration (FDA) does require an ingredient declaration on cosmetic products sold at the retail level to consumers (usually called the INCI list). However, certain ingredients may be listed generally as "fragrance," or "perfume," without identifying the specific ingredients, which can lead to manufacturers hiding certain ingredients in these generalized categories.

Cosmetics companies should, nevertheless, test their products for allergic reactions prior to releasing them to the market. Prior to launching a product that is intended to come into contact with a person's skin, it is imperative that it be tested to determine its likelihood of inducing an allergic reaction. The human repeat insult patch test (HRIPT) is the industry standard human clinical test used for personal care and pharmaceutical products to help predict the likelihood for induced allergic contact dermatitis (ACD) of topically applied products [4].



03. The four key elements of product stability testing: microbiological; physical/chemical; packaging; and accelerated aging.

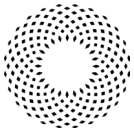
MICROBIOLOGICAL TESTING

Most skin care products, because they are intended to be used on a daily basis, are packaged in multi-dose containers, i.e., containers intended to be accessed numerous times. Each time a user accesses the contents of the container with their fingers, there is a risk that microorganisms present on their fingers may be introduced into the container and proliferate therein. Once contaminated, continued use of the product may lead to serious infections, particularly in people with compromised skin that is dry, cracked, and inflamed due to, for example, acne breakouts.

In an effort to avoid or mitigate contamination, preservatives are added to the products to prevent or limit microbial contamination. The effectiveness of the preservative system can be enhanced or diminished depending on the specific preservatives used. Preservative efficacy testing (PET) is the process used to evaluate the effectiveness of a preservative system in a cosmetic product. The results of such a test are critically important when evaluating the safety of a skin care product. The test involves purposefully introducing microorganisms into the product stored in its final retail packaging, i.e., inoculating the product, storing the inoculated product at a certain predetermined temperature, removing samples of the product at predetermined intervals of time, and counting the number of organisms present in the samples. Inoculated products are thus periodically tested over a 28-day period. The effectiveness of the preservative system is considered acceptable if there is an initial drop in the number of microorganisms present in the product to a predetermined acceptable level or no appreciable increase of microorganisms within the product during the testing intervals.

PHYSICAL AND CHEMICAL TESTING

The physical stability of a product is tested to evaluate its color, odor/fragrance, viscosity and signs of phase separation, all of which serve as clues of potential degradation over time. Changes in color may be a sign of degradation of active ingredients within the formula that can negatively impact the product's efficacy over time. For example, antioxidants, a class of highly efficacious active ingredients used for alleviating numerous types of skin issues such as aging, damage caused by environmental aggressors, and inflammation, are highly sensitive to UV light exposure. Over time, these ingredients tend to lose their potency due to their constant exposure to sunlight. Another physical property subject to stability testing is a product's viscosity (thickness). It's important that a formula maintain a consistent viscosity over its shelf life to ensure that it continues to properly flow out of its package and spread consistently over the surface of one's skin during use. Many cosmetic products, especially skin care products, employ a combination of water and oil in their formulas in order to hydrate the skin, and help seal moisture within the skin. Because it is well known that water and oil do not form a homogeneous mixture, ingredients known as emulsifiers are typically employed to facilitate formation of a single phase, homogeneous mixture. Over time, however, and depending on storage conditions (temperature/humidity/light exposure), a formula may separate, forming two or more distinct phases that, aside from its unsightly aesthetic appearance, can also negatively impact the product's efficacy since all of the ingredients in the formula may not be properly dispersed yielding inconsistent deposition of ingredients on the surface of the skin which can pose a potential safety issue.



The chemical stability of a beauty product must also be evaluated to ensure that there are no unwanted, potentially harmful chemical reactions occurring in the formula. As was mentioned above, over time ingredients present in the formula can decompose or cause unwanted chemical reactions to occur among the various ingredients that comprise the formula and/or with any contaminants that may be present therein causing unwanted compounds to be formed in the product. Products are therefore evaluated for the presence of any chemical indicators of degradation/contamination. For example, unwanted by-products of chemical reactions that occur in the formula may result in a change in the product's pH value, which determines whether a product is acidic or basic in nature. Another example is a recent study of sunscreens containing octocrylene that may produce benzophenone, a known carcinogen [5].

PACKAGING STABILITY

The final category of stability testing involves evaluating the compatibility of the product with its packaging. While a product may be stable and have a good shelf life when tested in a glass or other temporary container, that same level of stability may not be observed in the product's final packaging. It is therefore critically important that stability testing be performed on the product in its intended, final packaging as unwanted interactions may occur between the product, the package and the environment in which it is stored. Glass, though considered to be the least reactive packaging material, can nevertheless pose stability problems if it easily allows light to penetrate through its walls, resulting in degradation of ingredients such as antioxidants present in the formula that are highly sensitive to light and air. Moisture penetrating into, or evaporating out of, the package can cause various types of stability problems. The importance of choosing packaging that provides all of the protections the product contained therein requires, i.e., protection from light, moisture, air and other external contaminants that may impact the product's stability, shelf life and safety cannot be underestimated.

ACCELERATED AGING TESTING

Since the development cycle of cosmetic products is at times fairly short, "real time" stability testing is not always feasible. As a result, accelerated stability testing is oftentimes employed in order to more expeditiously perform the evaluation. Accelerated stability testing is typically performed under varying accelerated storage conditions where samples are stored at elevated temperatures over a period of 1-3 months. These types of accelerated testing conditions are recognized internationally as being acceptable at predicting a cosmetic product's shelf life. Testing protocols have been designed to determine a product's microbiological, physico-chemical and packaging stability in order to determine its quality, safety and performance characteristics. Factors tested at an accelerated rate include the above-mentioned color, odor, pH, viscosity and microbiological parameters relating to the efficacy of the preservative system used.

04. Allergy Testing: Human Repeat Insult Patch Test

The human repeat insult patch test (HRIPT) is the industry standard human clinical test used for personal care and pharmaceutical products to help predict the likelihood for induced allergic contact dermatitis (ACD) of topically applied products [4]. The test is performed over a 6-week period to determine the potential of the test product to induce sensitization in humans after repeated exposure. The product to be tested is applied onto occlusive or semi-occlusive patches, depending on the product type and its end-use. The patch is then applied onto the upper back of test subjects and is allowed to remain in direct skin contact for 24 hours, after which the subjects remove the patches from their back. Subjects then return 24 hours after patch removal for evaluation of the site and re-patching. This procedure is repeated 9 times over an approximate 3-week period, with patch applications and scoring of sites being done at predetermined time intervals. This is known as the induction phase of the study.

After a rest period of approximately 14 days, with no test product exposure, subjects return for what is known as the challenge phase. Test products are applied under the same patch type to a virgin site on the lower backs of the subjects and are removed approximately 24 hours later. The sites are then evaluated by expert clinical graders for any signs of reactivity immediately after patch removal, and then 48 hours and 72 hours after patch application, as well as at 96 hours if a reaction persists.
In general, minimal, transient reactions consisting of mild erythema, occurring during the induction or challenge phases, are indicative of irritation, and unless observed in more than a few subjects, are not clinically significant. Induced sensitization reactions may occur toward the end of the induction phase and/or only during the challenge phase and would include a more intense level of erythema (moderate to severe) with obvious edema at or beyond the patch site and are usually accompanied by a subjective complaint of itching.

05. Summary

Although product performance is understandably high on consumer priority lists, the importance of safety cannot be underemphasized in view of the fact that the product will be applied onto, and absorbed by, the user's skin. For that reason, it is imperative that proper safety testing be performed on a product prior to launch. This safety testing, in order to be considered comprehensive, involves not only testing the finished product itself, but also testing and evaluating the product's ingredients, manufacturing facilities/processes, stability and likelihood of inducing an allergic reaction. It is only after this level of safety-based due diligence is performed that a product can be released for public use.

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