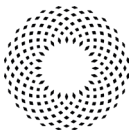
CODEX
BEAUTY LABS

Chapter: Product and Human Testing

SECTIONS



Stability Testing

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.

Stability testing of cosmetics generally encompasses evaluating three categories of product stability, namely, microbiological stability, physical/chemical stability and packaging stability. It is not until a product achieves satisfactory results in all of these categories that it can be considered safe to use over the course of its intended shelf life.

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 multiple times. Each time a person 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, once in, proliferate within the container rendering it contaminated. 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 extremely important when evaluating the safety of a skin care product. The test involves introducing microorganisms into the product stored in its final retail packaging ("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 removed from the container. 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 in microorganisms within the product over the testing period.

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 may affect the product's aesthetics, as well as provide clues of its potential for 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). Its 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 know 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. The odor/fragrance of a product need to also be evaluated to ensure that it does not develop an offensive odor/fragrance that can dissuade a consumer from wanting to continue to apply it onto their skin.

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.

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 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.

II. Human Testing

Today, the seemingly never-ending launch of new skin care products making compelling performance claims, by both established and indie brands, pose a dilemma for consumers, namely, how to determine what/who to believe. At the end of the day, it all boils down to testing. For example, claims such as "look 10 years younger" or "reduce the appearance of fine lines and wrinkles by 50%" can certainly cause consumers to purchase these products with the expectation that they will do what they promise/ claim. For those individuals inclined to believe the hype, its important for them to read the fine print. There is oftentimes an asterisk adjacent to such claims that indicate that these performance claims are based on "in-vitro" testing results. In the real world, there is a significant difference between "in-vitro" testing versus "in-vivo" testing.

The term "in-vitro" is Latin for "in glass" which means the product is tested on a glass substrate (e.g. glass dish) that is certainly NOT the equivalent of human skin. When a product is evaluated using in-vitro testing, the product is evaluated in a lab using skin cells cultured in a glass dish that represent the outermost layer of a person's skin. The main problem with in-vitro testing to assess a product's efficacy is that one cannot determine whether the product's active ingredients will effectively penetrate the outermost layer of a user's skin (epidermis/ stratum corneum) and reach the layer where the magic really happens, the dermis. Penetrating skin cells cultured on a glass surface is completely different from penetrating "actual" human skin.

One example of the deficiencies associated with in-vitro testing relates to a family of active ingredients found in wildly popular skin care products known as peptides. In the lab, i.e., on cells cultured in a glass dish, peptides have been shown to boost collagen production, reverse skin damage, lighten discoloration and make the cells look years younger. Unfortunately, these results are more often than not reproducible on actual human skin because most peptide molecules are too large to penetrate the outer layer (epidermis/ stratum corneum) of a person's skin, meaning, they cannot possibly deliver the real-life performance properties their in-lab testing would suggest.

"In-vivo" testing, on the other hand, involves application of a product onto animal and/or human skin in order to assess its true efficacy. However, since animal testing is prohibited in Europe, and frowned upon in most other developed countries, testing on live human subjects is the most accurate and transparent method of assessing a product's efficacy.

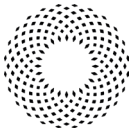
Prior to utilizing in-vivo efficacy testing, however, it must first be determined that application of the product onto the skin of human volunteers will not cause them to experience an allergic reaction or some form of painful irritation. This is done by performing what is known as a Human Repeat Insult Patch Test (HRIPT). This is an internationally recognized test used to determine the potential for irritation, sensitization and allergic reaction potential of a product. In view of the growing number of exotic ingredients used in skin care formulations, coupled with the increasingly complex and sophisticated chemical composition of the formulas, the risk of individuals experiencing irritation and allergic reactions because of their use has increased substantially. HRIPT is a skin patch test whereby patches containing the test product are applied multiple times onto the back of test subjects over a period of 6 weeks. This repeated contact with a potential allergen in the formula, if present, will generate a series of immunological reactions at the patch application site. Any allergic reactions experienced by the test subject will be observed, recorded and evaluated by a dermatologist to confirm, or not, the safety of the product. Once a product is cleared from an HRIPT safety/toxicology perspective, it can then be used for in-vivo efficacy evaluation.

In general, the type of in-vivo test to be performed depends on the claim being made by the product, i.e., if a product is touted as an effective skin moisturizer, then a test to determine moisturization will be conducted. The choice of the study design and type should take into account the nature of the claim/benefit being promoted. The main types of studies involved in cosmetic efficacy testing include: consumer studies; expert grading studies; and instrumental measurement studies. While consumer and expert grading studies involve a certain amount of "subjective/qualitative" evaluation, instrumental measurement studies are highly "objective/quantitative".

Instrumental measurements have been made possible by the advent of bioengineering techniques, and have continued to grow in importance in assessing skin characteristics. More particularly, the area of skin imaging has exploded in recent years with 2D and 3D image analysis devices and corresponding software being readily available to quantify parameters such as pore size; eye bags; depth of facial wrinkles; scalp hair and cellulite. All of the approaches provide "quantitative" results that can be further quantified as percentage variation (eg increased moisturization by 20%, reduction of wrinkles by 30%, etc). This quantitative data is often combined with qualitative data by way of a test subject self-assessment questionnaire.

Reliable studies should include several measurements to increase the study's robustness and the opportunity for secondary analysis. One or two outcomes, or "primary endpoints" should be chosen to assess the extent of the product's effect and to give proof of the claimed effect. For example, the efficacy of a moisturizing claim is properly assessed by the measurement of the stratum corneum's water content, while the measurement of a product's effect on skin barrier function is determined by measuring the amount of water evaporating from the surface of the skin.

Below are examples of in-vivo product efficacy evaluation parameters and instruments used to substantiate product efficacy.



Measuring Skin Smoothness and Anti-Wrinkle Effect

In-vivo testing of these two parameters involves the use of a fringe projection system known as DermaTOP®. This technique utilizes a fringe projector which shines light onto a person's skin surface at a certain angle that enables the height and depth if imperfections present on the skin surface to be captured by a camera, specially designed to be used in conjunction with the projector. The images captured by the camera are then evaluated by software that utilizes a specific algorithm designed to measure the height and depth of skin imperfections. When utilizing this technique, the height/depth of skin imperfections are first measured prior to use of the product to establish a baseline reading. Subsequent measurements are then taken at predetermined time intervals of use to determine what, if any, impact use of the product has had on the previously identified imperfections. If the product is doing its job of making skin smoother and less wrinkled, the height and depth of the imperfections will smaller following use of the product. Perfectly smooth skin such as may be found on a newborn infant, will have no imperfections. Wrinkled skin, on the other hand, will have imperfections of varying depth and height, which will be detected by the DermaTOP system. By measuring the distance between the height and depth of a wrinkles imperfection, both before and after use of a product being evaluated for efficacy, it can be determined what, if any effect, the product is having on the skin's imperfections (wrinkles).

Measuring Skin Firmness

If the product/claim being evaluated relates to skin firmness, then a system known as DynaSKIN®, which is an add-on to the DermaTOP® system, is utilized. The system is completely non-contact and utilizes air that is blown onto the surface of skin being evaluated, at an angle perpendicular to the skin's surface, to produce a deformation on the skin's surface that is evaluated to determine skin firmness. A dedicated software module computes the difference in the degree of deformation caused before and after use of a product being evaluated to determine whether the product is providing the intended effect. If the depth of deformation is less after use of the product, then it shows that the product has indeed improved the firmness of the skin. In principle, this system generates both visual and quantitative data, in a very reproducible manner that is similar to the real-world tactile perception of skin firmness, laxity and sag.

Measuring Skin Elasticity

A Cutometer® is an instrument used to simultaneously measure both skin elasticity and firmness. The instrument employs a suction-generating probe in combination with specialized software to assess both elasticity and firmness. The probe is placed on a small patch of skin and activated to generate a gentle suction, causing skin to be drawn into the probe, after which it is released and allowed to recover. The device measures the quantity of skin captured during the suction process based on how deeply and quickly the skin is drawn into the probe. This data point is used to assess skin firmness, it being understood that firmer skin will be more difficult, and take longer, to capture during the suction step. Once the suction step is concluded, the skin is released and allowed to recover with measurements being taken during the entire recovery process. The period of time it takes the skin to recover to its original state is used to assess skin elasticity, i.e., the longer it takes for the skin to recover, the less elastic it is. As a person ages, both the firmness and elasticity of their skin naturally decrease. When clinically assessing the efficacy of an anti-aging product on these biomechanical properties, the Cutometer® is a "go to" device for simultaneously measuring both skin firmness and elasticity, both before and after product usage.

Measuring Skin Hydration/Moisturization

When evaluating whether a product that claims its use will increase moisture/hydration levels provides the intended benefit, the use of a device known as a corneometer is typically used. In order to evaluate cutaneous hydration, the device relies on capacitance measurements. Water is well known as being an excellent conductor of electricity, i.e., has excellent capacitance. This device measures skin's degree of capacitance based on the humidity (moisture) levels present in the outermost layers of the skin being evaluated. If the skin's degree of capacitance increases (i.e., more electrical conductance is detected) after use of a product, its efficacy as a moisturizer is confirmed since increased electrical capacitance equals increased hydration/moisturization.

A corollary measurement for evaluating a product's hydration/moisturization abilities is known as Transepidermal Water Loss (TEWL). This measurement relates to the skin's ability to retain water. When water passes from the dermis, through the epidermis, and evaporates from the skin's surface, this phenomenon is referred to as TEWL and is a measure of skin's ability to retain moisture present in the dermis. TEWL is a process that the skin regulates naturally. However, if the skin's barrier function (ability to retain moisture) is compromised due to injury or exceptionally dry, TEWL levels can be negatively impacted. A person's skin requires both hydration and moisturization in order to maintain desirable levels of TEWL.

Measuring Anti-aging Effect on Skin

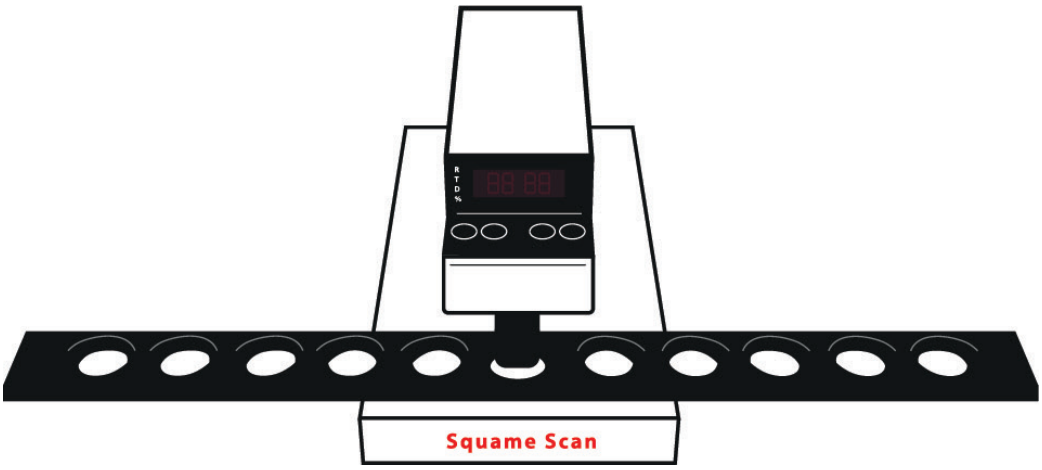
When performing in-vivo evaluations of the effects of an anti-aging product and/or active ingredient on skin, a device known as a Dermascan® C is typically employed. This device utilizes two-dimensional high-frequency echography to measure the distance between the dermis layer and epidermis layer of the skin. The device emits an ultrasound beam in order to generate a two-dimensional image of the space between the dermis and epidermis or, in other words, the thickness of the dermis/epidermis junction. As person ages, their skin naturally becomes thinner and thus more susceptible to damage. An increase in thickness of the dermis/epidermis junction indicates a positive anti-aging resulting in the skin looking better (plumper/younger) and being healthier due to its improved barrier function capabilities.

Measuring Redensifying Effect on Skin

An SIAscope is a device that utilizes intracutaneous spectrophotometric analysis in order to determine whether a product/active ingredient is effective at increasing the density of the dermis layer, indicative of an increase in the amount of collagen present in the skin. An increase in the density of the dermis corresponds to an increase in collagen present in the skin, thus evidencing the redensifying effect of the product/active being evaluated.

Measuring Restructuring Effect on Skin

A device known as a Squame Scan® is used to evaluate the barrier function of the external layer (epidermis/stratum corneum) of the skin. As skin ages, its barrier function capabilities decrease. In order for skin's stratum corneum to effectively protect the body from external aggressors like sunlight and pollution, as well as retain moisture within the skin to prevent it from becoming dry, it must possess a good barrier function. Skin's barrier function is directly related to the amount of carbonylated protein present within the stratum corneum. A decrease in carbonylated protein levels found in the stratum corneum corresponds to a restructuring effect of the skin that evidences an improvement in the skin's barrier function. Specially designed tape is first applied onto the surface of an individual's skin and then removed. Upon removal, dead skin cells taken from the stratum corneum are adhered onto the strip. The Squame Scan then measures the protein content present in the dead skin cells to ascertain the stratum corneum's barrier function, i.e., how well its performing its job of preventing the passage of unwanted external aggressors into the body, and the escape of moisture from the body. A decrease in carbonylated protein content present in the stratum corneum following use of a product indicates that it is successful in restructuring the skin, thereby enhancing its barrier function capabilities.



Measuring Sebum (oil) Control

Excessively oily facial skin is caused by overactive sebaceous glands and can affect both males and females. Those with this skin type have skin that is greasy, shiny, has large pores, and is prone to acne and seborrheic dermatitis. If a product is marketed as being useful for aiding those with oily skin, its ability to help inhibit sebum production is evaluated. Sebum production levels on a person's forehead and cheeks are measured using a photometric device called a Sebumeter. The quantity of sebum present on the mid-forehead is determined using sebum collector foils known as Sebufix, followed by evaluation with a skin camera called a Visioscope in conjunction with SELS (Surface Evaluation of the Living Skin) software. Measurements are taken prior to treatment and after several weeks of treatment (before and after treatment). A decrease in the amount of sebum present on the surface of the skin evidences the efficacy of the product.