TECHNICAL REPORT

ISO/TR 18811

First edition
2018-02

Cosmetics — Guidelines on the stability testing of cosmetic products

Cosmétiques — Lignes directrices relatives aux essais de stabilité des produits cosmétiques

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

Reference number
ISO/TR 18811:2018(E)

© ISO 2018

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

COPYRIGHT PROTECTED DOCUMENT

© ISO 2018

All rights reserved. Unless otherwise specified, or required in the context of its implementation, no part of this publication may be reproduced or utilized otherwise in any form or by any means, electronic or mechanical, including photocopying, or posting on the internet or an intranet, without prior written permission. Permission can be requested from either ISO at the address below or ISO's member body in the country of the requester.

ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva, Switzerland
Tel. +41 22 749 01 11
Fax +41 22 749 09 47
copyright@iso.org
www.iso.org

Published in Switzerland

© ISO 2018 – All rights reserved

Contents

Page

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

© ISO 2018 – All rights reserved

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 217, *Cosmetics*.

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

 © ISO 2018 – All rights reserved

Introduction

Stability studies are aimed at assessing the ability of a product to maintain the desired physical, chemical and microbiological properties, as well as functionality and sensorial properties when stored and used under appropriate conditions by the consumer. More simply, the objective of a stability study is to determine the shelf life of a product and to evaluate whether a product in the package is stable when subjected to the market conditions in which it is sold and used. The "market conditions" encompass distribution (transportation), warehouse storage and conditions during use.

Thus, the stability study may be seen as a prerequisite for ensuring product quality. Stability tests on cosmetic products are required for

— obtaining a guidance on the formulation of the product, and the appropriate packaging material,

— optimizing the formulation and manufacturing process,

— determining conditions of transportation, storage, display and manner of use,

— estimating and confirming shelf life, and

— ensuring customer safety.

This document identifies readily available references to assess the stability of cosmetic products on the market. Its purpose is to provide a resource for the selection of the appropriate stability tests. Although these guidelines provide a helpful starting point to evaluate new products and technologies, adapting the testing to reflect differences between product types and formulations may still be necessary.

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

© ISO 2018 – All rights reserved

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

Cosmetics — Guidelines on the stability testing of cosmetic products

1 Scope

This document gives guidelines for the stability testing of cosmetic products. It reviews readily available bibliographic references that provide a resource for the assessment of the stability of cosmetic products. This review of the available guidelines that assess the stability of cosmetic products can serve as a technical/scientific framework to identify the most suitable methods for the assessment of the stability of cosmetic products.

This document does not aim to specify the conditions, parameters or criteria of stability testing.

Considering the wide variety of cosmetic products, storage and use conditions, it is not possible to define a single way to assess product stability. Therefore, it is up to the manufacturer to specify and justify the stability protocol to cover test methods, specifications and conditions at which products will be tested.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— IEC Electropedia: available at http://www.electropedia.org/

— ISO Online browsing platform: available at https://www.iso.org/obp

3.1
accelerated stability evaluation
study designed to speed up naturally occurring destabilization processes due to intrinsic or extrinsic factors and which predicts the behaviour over the long term

Note 1 to entry: Typically, physico-chemical, mechanical or thermal procedures are employed.

3.2
real time stability evaluation
study that monitors the state of a product to determine the time course of any alteration to it under reasonably expected conditions of storage and use

Note 1 to entry: Often called “long term test” or “standard stability test”.

3.3
stability
ability of a cosmetic product to resist change or variation of its initial properties over time under stated or reasonably foreseeable conditions of storage and use

Note 1 to entry: See Reference [1].

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

© ISO 2018 – All rights reserved

3.4
stability criteria
deviations from initial properties or behaviour at production state, which are acceptable

Note 1 to entry: See Reference [1].

3.5
stability metrics
properties/parameters of the state or behaviour of a cosmetic product which should be monitored according to demanded, specific product qualities

Note 1 to entry: See Reference [1].

3.6
shelf life
recommended time period that a cosmetic product can be kept after its production, during which the defined quality of the product remains acceptable under expected conditions of distribution, storage, display and usage

Note 1 to entry: See Reference [1].

4 Basic principles of cosmetic stability

Design, formulation and the manufacturing process of cosmetic products have to fulfil general and specific demands and requirements of distribution pathways, and especially of customers. Specification, functionality and aesthetics have to be preserved, i.e. have to be stable, over the entire life cycle of a product.

Processed cosmetic products are complex matrixes which undergo spontaneous alterations to reach the free energy minimum in accordance with the second thermodynamic law.[2] These so-called intrinsic causes may be of physical, physico-chemical or chemical origin.[3] Many reactions and processes may lead, under the condition of the "market", to a deviation from the initial, original product properties at the date of manufacturing. Departure may be caused by thermodynamically driven internal or externally driven effects,[1] microbiological impact[4][5] or interactions with packaging[6] and may finally lead to a loss of specified product functionality or/and aesthetic attributes. This impacts usability, shelf life and marketability. Destabilization processes of the original product may also be provoked, enhanced or magnified due to extrinsic (external) factors. For example, state changes may be triggered by thermal energy loss or gain, light and UV irradiation, mechanical energy input (such as vibration or pressure), oxygen uptake, humidity, interaction by or with container/closure system (packaging), and proliferation of microorganisms.[3]

Cosmetics are of different natures and some consist of several phases, dispersed ones and a continuous one, and may be classified as suspensions or emulsions. Suspensions are solid particles dispersed in a liquid phase. Emulsions are composed of two liquid phases, typically oil-in-water (o/w) or water-in-oil (w/o). Cosmetic dispersions are usually very complex and may contain several phases.

A stability test aims at providing information on the state/behaviour of the cosmetic products in the container/enclosure under the different conditions to which they may be subjected from their manufacturing date until the end of their recommended period of use.[7][8][9] The state of a cosmetic product and its stability depend upon numerous interrelated physical, physico-chemical and chemical parameters as well as interaction with environment, and its nature is therefore very complex. In general, they may be roughly classified as mechanical-driven, thermal- or diffusion-driven, interaction-force- driven or externally provoked processes.[1][7][10][11] There is no universal method or technique to quantify all stability aspects due to the complexity of different pathways of destabilization. Therefore, it is always necessary to specify precise stability metrics and acceptance criteria.

After determination of the stability metric(s), it is necessary to select appropriate stability test methods to monitor the alteration of the product over time. It is recommended to select methods that do not require sample preparation (e.g. dilution) and quantify kinetics of the product destabilization based on defined metric(s) in a direct way.[1] Real time measurements can be made by traditional visual

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

© ISO 2018 – All rights reserved

observations, sensory techniques or use of different measuring techniques which are advantageous in being quantitative, objective, traceable, reproducible and retrievable.[1] Scanning and spatially resolving techniques are appropriate in particular to detect phase separation and help to discriminate between phase separation and phase changes.[1][7][10][11]

In the case of very stable products, analytical techniques having high resolution/sensitivity should be used and procedures can be required in order to accelerate the alteration to shorten the detection time to meet the predefined stability criteria.[1][11] Typical acceleration approaches are mechanical ones (e.g. high gravity by centrifugation) or elevated storage temperatures for a given time. Preservation efficacy testing (challenge-test) aims to test microbiological attributes under accelerated conditions.[3][5] However, because of the interrelated physical, physico-chemical and chemical properties of cosmetic emulsions or suspensions, adequate acceleration methods may be chosen and verified in the context of a specific product.[1][11]

Beside direct methods, correlative test methods are utilized focusing on determination of a single parameter of the state of a product that is known to correlate with product stability.[1] Typical parameters measured and compared with pre-defined acceptable values are, for example, mean particle/droplet size or zeta-potential. These quantities reflect the state at the time of the measurement and do not yield kinetic information. Such test procedures may be used for quality assessment of a specified product but, due to the complexity of the state of cosmetic products, currently no theoretical basis exists to predict the time course of any product alteration based on a single parameter obtained at any single time point. In addition, most of these measuring techniques demand sample preparation and often product dilution.[1]

Due to the cosmetic product formulation's complexity overall, caution should be employed in stability assessment and predicting its shelf life, and the properties of the constituents should be considered and understood, as well as the product's behaviour and the factors which influence it.[11]

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

5 Aspects to be addressed during stability testing

5.1 General

The key aspects to consider when assessing the stability of cosmetics products are listed in 5.2 to 5.6. Guidance is provided based on the review of relevant sources cited in the text.

5.2 Stage/scale of tested batches

When working on a brand new product (new formula, new manufacturing process, new packaging) and therefore where no significant body of knowledge is available, it might be appropriate to carry multiple independent stability studies, usually referred as "preliminary tests". It is up to the manufacturer to decide on the number of batches, the scale of their manufacture that are subject to stability testing and at what stage of the project development cycle this takes place.[7][12][9][13]

The stability of the final product (final formula, final manufacturing process, final packaging) may be demonstrated before its commercialization. Accelerated stability evaluation may be conducted prior to commercialization to predict product shelf life. Following commercialization, the shelf life confirmation is obtained by long term stability testing on representative formulations.

Minor variations between products subjected to stability testing versus final commercial product can be acceptable if they are deemed as not having an impact on product characteristics and integrity, but need to be documented and justified.[9]

Common acceptable practices include but are not limited to

— usage of formulation samples from the development stage for preliminary tests,

— usage of pilot batches instead of production scale, for some specific non-scale up products and where the manufacturing process is considered equivalent,[13][14] and

© ISO 2018 – All rights reserved

— usage of unlabelled packaging, or packaging of different shape, when packaging size, closure system and material remain unchanged, or when decorative material remains of same nature but with different design (e.g. same ink versus different print).

Additionally, matrixing and bracketing[14] are acceptable practices but should be documented and justified to ensure that the stability study protocol will cover the entire product portfolio and provide enough information (e.g. multiple shade, packaging size).[13][14][15]

5.3 Test procedures and conditions

5.3.1 Principle

The general objective of a stability test is to determine whether a given product, in the container in which it is being marketed, has an adequate shelf life, under the conditions of the market in which it is being sold.[16]

Stability testing may be of sufficient duration to cover storage, shipment and subsequent use, and to guarantee safety and quality.

Manufacturers may, for each formula type, select the pertinent test criteria according to their experience and evaluate these test criteria at one or more temperatures.

Because of the wide variety of cosmetic products and their inherent complexity, standard stability tests cannot always be prescribed.[7] Both real time and accelerated test procedures are used to provide the desired information. Most cosmetics, due to their short development cycles, require accelerated test protocols to help predict stability parameters in a shorter period of time. To achieve these end points, some samples are kept under test conditions designed to accelerate changes that may occur and some are stored at normal conditions. Test conditions refer to the various manufacturing or storage conditions (e.g. batch) or combination of conditions (e.g. container closures) to be studied.[10] The recommended shelf life may be estimated by accelerated stability tests and can be confirmed by real time (long term stability) tests.[13]

While shelf life is determined by the stability of the product, the overall stability profile is made up of several components, such as

— the inherent chemical and physical stability of the product, and

— the possible interactions between the product (contents) and its primary packaging.

In order to generate the desired information recommended, standard/long term and accelerated test parameters are outlined in 5.3.2 to 5.3.6.

5.3.2 Temperature and humidity

NOTE See References [10] and [16].

Accelerated and long term conditions can be used. The long term condition is conducted at regular storage conditions (e.g. controlled room temperature), while the accelerated testing is conducted under stress conditions (e.g. elevated temperature) which aims to increase the rate of potential degradation. [3][7][8][9][10][12][13][16]

Throughout this document it is assumed that all temperature and humidity storage conditions might experience a variation, for example ±3 °C and ±5 % RH.

Accelerated test conditions may vary and should be established based on correlations to real time storage conditions for the specific region or market. References to commonly used accelerated test conditions for testing cosmetic products are provided in the Bibliography. The temperature used and the duration will depend on the product type.[3][7][10][13][16][17][18][19]

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

 © ISO 2018 – All rights reserved

Samples stored at elevated temperatures represent a more constant degree of acceleration and render stability predictions as being more accurate. Cosmetic stability guidelines list various storage conditions and durations for accelerated stability testing:[3][16][17][19]

— (30 ± 2) °C;

— (37 ± 2) °C;

— (40 ± 2) °C;

— (45 ± 2) °C;

— (50 ± 2) °C.

Durations range from one week to three months. Relative humidity may be ambient[16] or controlled, such as 37 °C to 40 °C/75 % to 80 % RH.[9][17]

Alternative temperature and humidity conditions may be used, including an intermediate condition of (30 ± 2) °C and 65 % RH.[9][14][20] Test conditions and durations may be adjusted where justified to cover the product's distribution and storage conditions.[9][18]

Instability can be caused by either chemical reactions or physical processes and often a combination of both. These alterations proceed at a faster rate at higher temperatures but the degree of acceleration is variable as it depends on the specific rate constants, which are often unknown. Care should be taken in the interpretation of results when using temperatures far removed from ambient, as the observed changes may never occur at normal in market temperatures. Use of moderate elevated temperature, e.g. 37 °C to 40 °C, is a more realistic condition for predicting in market stability.[10][17]

Tests at low or elevated relative humidity are normally tests of the package and not of the product. They serve either to show the effect of storage at varying humidity on the container or as a measure of the barrier properties of the container. Products may be adversely affected by atmospheric humidity but if this happens in the product in its sale package it indicates that the package provides inadequate protection from the atmosphere.

Tests at elevated humidity are less likely to accelerate changes at normal storage conditions compared to tests at elevated temperatures and ambient humidity. If absorption of water vapour presents a risk to the packaged product's properties, then testing at elevated humidity may accelerate changes. If the risk is loss of water or other volatile constituents (such as in permeable packaging), then elevated humidity may actually retard changes, and testing at low humidity may be more appropriate.

It may be appropriate to consider low temperature storage during stability testing.

— Refrigeration at 5 °C (2 °C to 8 °C) / ambient humidity: This condition may be used to store samples to be used as reference samples.[3]

— Freezer at −5 °C to −10 °C: This condition may be used to determine the effects of extreme low temperature, for example during transportation.[3]

5.3.3 Cycling of temperature and/or humidity

Tests in which the temperature and/or humidity are changed at regular intervals, and which subject the package to variations other than static stresses, are sometimes more severe tests than continuous storage at one condition. These tests provide evidence of emulsion stability, tendency to crystallization, deposition or clouding, and whether the reaction is reversible. This data are also applicable to determining how robust a product is to extreme fluctuations in temperature during distribution and storage.[3][10][16][19]

Freeze/thaw tests are applicable to

— liquid products as a measure of the potential to develop crystallization or cloud formation, and

— emulsions or creams as an indicator of emulsions stability.

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

© ISO 2018 – All rights reserved

Freeze/thaw tests may be carried out on all solutions, emulsions, creams and all other liquid or semi-solid products. These tests provide evidence of emulsion stability, tendency to crystallization, deposition or clouding, and whether the reaction is reversible.

Typical conditions for freeze/thaw cycling are: 12 h to 24 h at freezing temperatures (e.g. −5 °C) followed by 12 h to 24 h at thawing temperatures (e.g. 25 °C) or elevated temperatures (e.g. 45 °C) for a specified number of cycles.[10] Suggested cycling conditions include the following limits:[3]

— 24 h at (25 ± 2) °C and 24 h at (−5 ± 2) °C;

— 24 h at (40 ± 2) °C and 24 h at (4 ± 2) °C;

— 24 h at (45 ± 2) °C and 24 h at (−5 ± 2) °C;

— 24 h at (50 ± 2) °C and 24 h at (−5 ± 2) °C.

The number of cycles may vary, for example six cycles can be used.[3]

5.3.4 Vibration

Testing is conducted in order to examine the changes in quality under severe conditions that may be encountered during distribution such as temperature extremes, shipping and light. One example of stress testing would be vibration tests. Vibration tests may be needed to determine if emulsions or powders are going to break or collapse during transport. Vibration tests on a suitable vibrator of known frequency and amplitudes for a specified period of time and temperature (room temperature and/or elevated temperatures) may be carried out in appropriate instances. It is preferable to treat different samples with different frequencies and amplitudes of vibration using either an orbital or vertical shaker.[3][10][16]

5.3.5 Centrifugation

Emulsions and suspensions may be centrifuged as a means of testing its vulnerability to destabilization phenomena like phase separation, caking, bleeding and segregation.[1][3][10][16] Centrifugation increases gravity force acting on product constituents of different density. It is suggested to apply slight or moderate elevated gravity[9][10] for a given time depending on shelf life expectations of the cosmetic product. Appropriate measuring conditions to start can be estimated by equating the expected shelf life to centrifugation time (same units as shelf life) multiplied by the relative centrifugal acceleration (centrifugal acceleration divided by earth acceleration, RCA).[1][3][10][11] Test time depends inversely on applied RCA. In order to ensure the most accurate prediction of stability and shelf life, the user may increase measurement time by decreasing RCA. Chemically driven destabilizations may be tested by a combination with prior storage at elevated temperatures and subsequent centrifugation.[1][10][11]

5.3.6 Exposure to light (photostability)

Exposure to light can bring about change in products. If relevant, the product can be tested in clear containers to determine the need for protective packaging and also in its finished package. The objective is to determine the effect of light exposure on the unprotected product (if packaged in clear or semi- transparent packaging) and the effect on the package (discoloration, stress cracking). The lighting used in testing can simulate the intensity to which the cosmetic will likely be exposed during storage on store shelves or in consumers' homes.[1][7][19]

The effects of exposure to light are difficult to accelerate. The source of illumination may have the same spectral distribution as daylight (window filtered) and other room light sources (such as fluorescent, incandescent). It is often difficult to assess the extent exposure to light that samples receive in the market and therefore estimate the degree of exaggeration or acceleration that any one test gives. For example, the product may be exposed to daylight (window filtered) or artificial room light (fluorescent, incandescent).

Protected samples (kept in the dark or wrapped in aluminium foil) may serve as controls in order to evaluate any contribution of thermally induced changes over the same period of time.[12]

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

 © ISO 2018 – All rights reserved

Test conditions mentioned in the relevant reference documents are natural sunlight or window test. Exposure to direct sunlight is to be avoided since products are seldom exposed to it and can produce reactions that are not normally seen in practice. A problem inherent to this type of testing is to quantify the extent of the exposure that samples have received. Daylight varies with location, season and weather.[3][16] Alternatively, continuous exposure may also be done with photostability testing equipment. The ICH Q1B photostability guideline may be used as a reference for testing cosmetic products and packaging.[12]

5.4 Physical, physico-chemical and chemical alterations

5.4.1 Physical destabilization phenomena of different product types

5.4.1.1 General

In general, in addition to the causes detailed in this clause, destabilization may be the result of change in state of the formula due to microbiological factors as well as due to evaporation and interaction with the packaging materials. For the latter see 5.5 and 5.6.

Physically driven phenomena are, for example, phase separation, precipitation of ingredients, segregation of particles or droplets differing in their properties, and bleeding of oil or water phase, as well as changes of the dispersed phase state such as Ostwald ripening, coalescence, flocculation and agglomeration, and phase inversion up to initiating slow structuring processes (gelation, network formation). These phenomena affect not only product specification and aesthetics but also separation and distribution, for example, of UV-blockers of a sun protection cream in a hot environment which would cause serious risk for customer.

5.4.1.2 Dispersions (emulsions and suspensions)

Dispersions consist of disperse phase(s) and a continuous phase. Emulsions and suspensions are thermodynamically unstable.[2] Their stability may be prolonged through optimization of the formulation and process. In characterizing a dispersion, it is important to understand the type of dispersion (suspension, oil/water emulsion, water/oil emulsion), the nature of the disperse phase(s) and the continuous phase, the particle interactions (attractive and repulsive forces), barrier properties at the interface between droplet or particle and the continuous phase, and what phenomenon can lead to de-mixing, segregation or even gelation. Upon understanding these characteristics, an appropriate stability metric(s) should be defined and, based on this, the corresponding stability study should be designed.[1][10][11]

ISO/TR 13097 provides further guidelines with references for characterizing dispersion destabilization. Types of demixing phenomena include coalescence, flocculation/agglomeration, creaming, flotation, phase inversion, phase separation and settling/sedimentation. Interactions between particles or between particles and ingredients in the continuous phase may result in changes to the state of the dispersion.[1][2][17]

5.4.1.3 Pressed and loose powders

Settling and segregation of powders affect the product's homogeneity. Humidity may affect its flowability. These product characteristics depend on size, shape, surface roughness and density of particles and endanger product quality, especially for broad distributions of such particle properties or different particle types.

5.4.1.4 Semi-solid and wax based products (pencils, lipsticks, lip gloss)

Temperature changes influence the miscibility of the formula ingredients. In the worst case, exceeding the melting points of structure forming ingredients will largely impact product aesthetics. Temperature changes and especially fluctuations may lead to syneresis (liquid bleed) or bloom. In this case, one or more ingredients may be less soluble in the sample matrix and migrate to the surface of the product where the ingredients (usually oils and fatty materials) may or may not re-absorb back into the sample.

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

© ISO 2018 – All rights reserved

5.4.1.5 Solutions (fragranced hydroalcohol products, toners, fresheners)

Particular attention may be given to the formation of precipitate or change in turbidity over time, either due to solubility issues (which may be altered at different temperature conditions), or due to ingredient interactions. Freeze/thaw and temperature cycling or swing tests provide conditions which may trigger precipitate formation.

5.4.1.6 Gels (shower gels or body wash products)

Similar to solutions, precipitates may develop over time due to solubility or ingredient interactions. Increasing the temperature may not redistribute the phase. A breakdown of the gel network structure formed by polymeric additives can result in loss of viscosity.

5.4.1.7 Fragranced formulations (solutions, gels, soaps)

Fragrance components may precipitate out of solution, which can impact the aroma of a fragranced product. Stability tests may include a control (unfragranced product) alongside the test sample(s), if determined to be necessary by the laboratory.[21]

5.4.2 Chemical destabilization processes

5.4.2.1 General

Chemically driven alterations of the state of cosmetic products, on the other hand, are due to chemical degradation or changes of molecular structure of molecules of continuous phase, of constituents of particles, especially alterations at the emulsion interface as well as of any stability or functional related additive. Typical reactions are hydrolysis, oxidation or transesterification.[3][10][16][17][21] These reactions may trigger breakdown of stabilizing surfactant and emulsifier, hamper functional polymer additives or deactivation of preservatives used to inhibit microbial growth.[1][10] Chemical reactions also may create active sites which may further promote structuring changes, such as gelation (desired or undesired) and result in further changes to physico-chemical properties, such as pH, colour or odour.[21] Further explanations of these factors are discussed in the ANVISA guideline on stability testing of cosmetic products.[3]

5.4.2.2 Oxidation

Oxygen can lead to the formation of free radicals, setting in motion oxidation–reduction reactions. Oxidation–reduction reactions may cause changes in the concentration of active ingredients and also in the organoleptic and physical characteristics of the formulation.[3] For example, the following processes may occur: unsaturated lipids are oxygen-labile; olefinic bonds can readily undergo fermentation resulting in volatile and nonvolatile aldehydes, acids and alcohols, as well as multiple radicals which can propagate further reactions. Trace presence of metals, such as copper, manganese or iron may also initiate or catalyse oxidation reactions.[10] Many fragrance ingredients are sensitive to oxygen exposure and may be even more prone to oxidize, particularly if accelerated by heat or light.[21]

5.4.2.3 Light alterations

Light may induce photoreactions and UV light may also trigger formation of free radicals. Products containing light sensitive molecules can be protected from light by packaging them in dark or opaque containers.[3] UV inhibitors in the formula (or packaging) may help to retard these light-induced reactions.

5.4.2.4 Hydrolysis

Hydrolysis occurs through reactions with water. Esters and amides are more susceptible to hydrolysis; a higher percentage of water in the formulation make the product more vulnerable to hydrolysis.[3] As with oxidation, these reactions may impact the aesthetic or physical attributes of the product. For

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

 © ISO 2018 – All rights reserved

example, hydrolysis of a surfactant can lead to the separation of an emulsion or loss of cleaning efficacy of a cleanser. Decomposition may generate undesirable by-products that can be irritating to the skin.[17]

5.4.2.5 Transesterification

Transesterification results as the reaction between the ester function of one molecule with the parent hydroxyl group of an alcohol. With fragrances and flavours, this type of reaction may alter the odour or taste.[21]

5.4.2.6 Interactions between ingredients

Chemical interactions between functional ingredients and formula excipients or between fragrance oil and product excipients may include discoloration, the development of off-odours, insolubility, viscosity and texture changes. These reactions are typically triggered by light, heat, oxygen, salt or pH. Schiff base formation occurs when an aldehyde (for example, from fragrance oil) reacts with a primary imine or amine to release a water molecule, forming a highly coloured Schiff base and resulting in marked different colorations of the product. Other ingredient interactions may include polymerization, which is typically triggered by oxygen. The outcome of polymerization may impact the product's viscosity and texture.[21]

5.4.3 Destabilization phenomena

The above processes describe phenomena which are relevant to products such as cosmetic solutions, lotions, ointments, soaps, lipsticks or creams. The breakdown of a surfactant through hydrolysis or biodegradation can lead to the separation of an emulsion or the loss of effectiveness of a facial cleanser.[1] The degradation of a preservative can result in microbial growth, thus affecting the consumer's safety and may also lead to observable physical changes in the product.[1][10] Even minor chemical changes may result in unacceptable colour and odour alterations to the product, whereas physical changes, such as precipitation of ingredients or liquid bleeding from emulsions or suspensions, may affect the product's properties and aesthetics such that the product shelf life is shortened and may be no longer marketable.[17]

Stability studies may include stability indicating tests for attributes that are susceptible to change and which may impact the physical, chemical, and microbiological properties of a product.[4] In other words, stability metric(s) determines appropriate test methods to be used to characterize a cosmetic formulation. Its general objective consists in being able to monitor relevant alterations of the state of a given product and to quantify kinetics of destabilization. Kinetic data may be employed to predict shelf life.

Methods should be specific and sensitive for the metric(s) of interest, as well as accurate and precise. They may avoid any sample preparation[1], as this may alter the state of the sample to be monitored. If sample preparation cannot be avoided, care should be taken to prepare samples.

When applicable, verified stability test methods should be applied. ISO/TR 13097 references specific methods to characterize emulsions and suspensions by visual methods (subjective, qualitative, with or without microscope), direct instrumental methods (objective, quantitative, such as transmittance or backscattering, conductivity, electroacoustic spectroscopy), or correlative methods (e.g. steady or dynamic rheology, particle size distribution or zeta potential). However, in the latter case often sampling and sample preparation cannot be avoided.[1] Quantitative chemical analysis for key ingredients should ensure the methods are specific for the compound of interest.[1][17] In general, test methods may be tailored to the specific product type (e.g. dispersion, soap, fragranced alcohol product, gels, body wash, lipsticks/lipgloss, pencils).

Procedures may be necessary to accelerate the evaluation of long-term stability to shorten test time in research and development and pre-shipping quality control. Mechanical, thermal or physico-chemical procedures are well known.[1][2] For example, the Arrhenius equation supports the use of elevated temperatures for accelerated stability testing. It relates the rate constant k for a chemical reaction and temperature T (degrees K) and may be used to predict the rate of the reaction at different temperatures by measuring the rate at higher temperatures.[10] Given the variety and complexity of cosmetic formulations and their packaging, accelerated testing may trigger additional further destabilization

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

© ISO 2018 – All rights reserved

phenomena which would not typically be observed under normal conditions of storage and use.[1] ISO/TR 13097 advises to decrease the intensity of the accelerated conditions to extrapolate the data to normal storage conditions.[1][11]

Accelerated testing may always be considered regarding its limits and its correlation to normal shelf life conditions and/or typical usage. Accelerated test results may be verified through real time (long term) stability testing.[1]

5.4.4 Specific test methods

5.4.4.1 Organoleptic tests

General organoleptic tests may always include visual observations (with or without microscope) for appearance, texture, consistency, bloom, precipitation or syneresis (liquid bleed). Clear or translucent solutions and gels may be evaluated for clarity. Changes in any of these attributes can be the result of physical or chemical interactions as well as of microbiological processes. In addition, the product may be examined for changes in odour/taste and colour, as these are indicative of chemical changes. A grading system (either numerical or descriptive) may be devised to more objectively characterize the degree of these changes.[3]

5.4.4.2 Direct instrumental methods to monitor physical and physico-chemical alterations due to destabilization

Instrumental methods may be used as deemed necessary to supplement visual and organoleptic stability evaluations in order to objectively quantitate changes in the product's physical characteristics in real time. Examples include measuring transmission, conductivity, ultrasound, photographic digitizing methods, X-ray, or other optical techniques.[1][11] Methods employed are as follows.

— Profiling of transmission or backscattering intensity or extinction over entire sample height to analyse and rank creaming, sedimentation, phase separation and phase alterations.

— Determination of conductivity or sound propagation property changes at different positions (e.g. near top and near bottom) to detect alteration in the state/composition.

— Detection of changes of overall product homogeneity as well as separation/segregation of dispersed phase by methods applicable to analyse high volume concentrations.

— Turbidity alterations analysed simultaneously by different wavelengths to characterize change of particle size by turbidity index.

— Determination of formation of cream or sediment layer thickness by optical or X-ray methods.

— Progress of clarification or turbidity in regions of interest along the sample height and quantification by an appropriate instability index.

5.4.4.3 Correlative instrumental methods to measure physical properties and chemical alterations of a product

The following methods are often used to compare samples of different batches or a new formulation with a reference.

— The pH value and its alteration provide an indication of chemical and microbiological changes, such as hydrolysis of an ester. Note that the pH can only be measured in aqueous continuous phases.

— Viscosity, measured at a standard temperature representative of the ambient temperature of the target market and using relevant equipment settings.

— Microscopic and electron microscopic analysis of small volume of cosmetic samples to provide structural, morphological and compositional information.

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

 © ISO 2018 – All rights reserved

— Rheology (steady or dynamic shear rates) to provide information on a formulation's shear dependent or viscoelastic behaviour and gives insight into changes to structure of dispersions, semi-solid pastes, ointments and gels.[2]

— Density determination of disperse and continuous phase to quantify or quality check amount of weighting agents and to provide information on changes in homogeneity and/or incorporation or loss of air or volatile compounds.

— Electrophoretic mobility and, if requirements apply, Zeta-potential to judge electrostatic driven particle interaction as part of total interaction forces.

— Mean/median particle size or size distribution analysis to assess the microscopic behaviour of the particles or emulsion droplets (disperse phase). A remarkable increase in particle size is a good indicator of coalescence or agglomeration/flocculation. Smaller changes may indicate Ostwald ripening.

— Number (concentration) of particles or droplets larger than a stated size value to meet sensory properties and avoid enhanced onset of coalescence or agglomeration/flocculation.

— Penetration or texture analysis to evaluate hardness and softness of semi-solid pastes and anhydrous, waxy pigmented and unpigmented products.

— Thermal analysis to quantify melting point, drop melting point, softening point and/or solidification/crystallization temperatures or phase inversion point of appropriate cosmetics (e.g. anhydrous semi-solid waxy pastes). Differential scanning calorimetry (DSC) may be used and serves as an indication of morphological changes of the formulation's components.[10]

— Weight loss of the product in the final package intended for market to determine the effectiveness of the container/closure's barrier properties and seal integrity.

— Assay methods may be conducted using a variety of chemical or instrumental techniques, such as chromatographic or spectrophotometric methods, for qualitative or quantitative analysis.[11] In relation with microbiological issues, preservatives may also be assayed to supplement the microbiological challenge testing.[10]

5.4.4.4 Procedures to accelerate stability testing and evaluation

Stable products exhibit very slow alterations in real time and therefore procedures may be required in order to accelerate the alteration to shorten the measurement time to classify products regarding its stability.[1][11] Test results based on these approaches should be verified by real time stability testing under normal conditions.[1][10]

The following points should be considered.

— Storage of the product at elevated temperatures and varying humidity may be used to accelerate physical (e.g. diffusion, viscosity) and chemical changes.[10]

— Vibration (at different frequencies and amplitudes) may result in the collapse of a foam, the settling of powders, or the destabilization of a dispersion. Gentle agitation of some emulsions may either decrease the apparent viscosity (shear thinning behaviour) or increase the number of collisions between particles, rendering the rate of their interaction.[10]

— Tests at higher than earth gravity by analytical photocentrifugation enhances all physical driven destabilization phenomena (creaming, sedimentation, sediment and cream layer formation, segregation, bleeding and ringing) as well as particle-particle interaction phenomena. These predictive tests prove to be valuable when optimizing formulae and processes as well as for QC before shipping.[3][11]

— Application of very high gravity (e.g. ultracentrifugation) may be appropriate to characterize critical forces to induce aggregation or coalescence, to overcome network formation or gel stabilization.[11]

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

© ISO 2018 – All rights reserved

— Change of physico-chemical characteristics of cosmetic samples by salt addition, surfactant or emulsifier "inhibitors" or pH shifting additives may be a sensitive test to figure out stability limits.[14] Freeze/thaw and climatic cycling can be used to detect destabilization of dispersions which have a tendency to coalesce, e.g. o/w emulsions.[11]

5.5 Microbiological aspects

5.5.1 General

Most of the references dealing with the stability of cosmetic products mention the microbiological attributes as key parameters to be tested as they are susceptible to change during storage and are likely to influence safety and/or quality.[4][17]

5.5.2 Microbiological parameters

The microbiological parameters for stability testing are

— microbial count, and

— preservation efficacy testing (challenge-test).

The methods to be used for the evaluation of those parameters indicated in the Bibliography are those described in the pharmacopeias[3][4][5][16][22] or CTFA guidelines.[3][10] Microbiological methods relevant for cosmetic products are described in the following International Standards on cosmetics microbiology:

— ISO 11930;

— ISO 16212;

— ISO 18415;

— ISO 18416;

— ISO/TR 19838;

— ISO 21148;

— ISO 21149;

— ISO 21150;

— ISO 22717;

— ISO 22718;

— ISO 29621.

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

5.5.3 Testing conditions

Stability studies are generally performed under accelerated conditions, and, in parallel, under real conditions. Some reference documents provide guidelines on the approaches to be used but selecting uniform test conditions is difficult as there are various factors that affect the stability of cosmetic products[18], e.g. product category, formulation type, composition (internal factors), manufacturing process, temperature, humidity, sunlight and packaging materials (external factors).

Regarding microbiological stability, the presence of water in the composition is considered as a key factor: emulsions, solutions and suspensions[4][8] may be submitted to a microbiological analysis while products such as powders,[8] nail varnishes, products with water activity (aW) ≤ 0,75 or alcohol content ≥ 20 %, synthetic detergent bars and soap bars can be exempt (see, for reference, ISO 29621).

© ISO 2018 – All rights reserved

For susceptible products, it is generally recommended that challenge tests (including microbial counts) being carried out at T0 and at the end of the stability testing[8][22][23] and/or after the accelerated study period.[3][5] Analysis of preservative content may be performed in parallel.[16][22][23]

5.5.4 Microbiological specifications

Acceptance criteria are numerical limits, ranges and other criteria for the specific tests described.[4][5] Microbiological specifications relevant for cosmetic products are provided in in the following International Standards:

— ISO 11930;

— ISO 17516.

Besides International Standards on cosmetics microbiology, some countries or regions can have legal requirements on microbiological content for cosmetics.

5.5.5 Interpretation of results

Microbiological changes such as growth of microorganisms and change in the efficiency of the antimicrobial preservation are likely to impact the safety and integrity of the final product.[22] Therefore, it is expected that products continue to show adequate antimicrobial efficacy at the end of the shelf life.[16][22]

5.6 Interaction with packaging

5.6.1 General information

Different package materials can be evaluated in order to determine the most adequate alternative for the product. Tests can be carried out in parallel with the stability tests and under the same conditions, to verify the possible interactions between the product and the package material with which it is in direct contact, such as absorption, migration, corrosion and other phenomena that may affect the integrity of the product.[1][7]

Since this is usually a destructive test, it is necessary to accurately establish the number of additional samples to be stored and evaluated.

5.6.2 Types of packing materials and main possible evaluations

NOTE See References [6] and [13].

5.6.2.1 Cellulosic material (paper, cardboard)

Evaluations can include those of structural alterations in the paper and the formulation, which are likely to lead to a component migration resulting in the contamination of the product, package physicochemical stability, appearance and functionality of the package, and barrier function (e.g. oil, water and gas permeability).

5.6.2.2 Metallic materials

Evaluations can include those of laminated materials (where applicable), corrosion, appearance and functionality of the package, reaction to the formula, integrity of the varnish or resin (whether internal or external), determination of metals, and, where applicable, functionality.

STANDARDSISO.COM : Click to view the full PDF of ISO/TR 18811:2018

© ISO 2018 – All rights reserved