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Kosmetik – Mikrobiologi – Retningslinjer for risikovurdering og identifikation af produkter med lav mikrobiologisk risiko

Cosmetics – Microbiology – Guidelines for the risk assessment and identification of microbiologically low-risk products

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Cosmetics - Microbiology - Guidelines for the risk assessment and identification of microbiologically low-risk products (ISO 29621:2010)

Cosmétiques - Microbiologie - Lignes directrices pour l'appréciation du risque et l'identification de produits à faible risque microbiologique (ISO 29621:2010)

Kosmetische Mittel - Mikrobiologie - Leitlinien für die Risikobewertung und Identifikation von mikrobiologisch risikoarmen Produkten (ISO 29621:2010)

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Foreword

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The text of ISO 29621:2010 has been approved by CEN as a EN ISO 29621:2011 without any modification.

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Foreword

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ISO 29621 was prepared by Technical Committee ISO/TC 217, *Cosmetics*.

Introduction

Every cosmetic manufacturer has a dual responsibility relative to the microbiological quality of its products. The first is to ensure that the product, as purchased, is free from the numbers and types of microorganisms that could affect product quality and consumer health. The second is to ensure that microorganisms introduced during normal product use will not adversely affect the quality or safety of the product.

The first step would be to perform a microbiological risk assessment of the product to determine if the cosmetic microbiological International Standards apply.

Microbiological risk assessment is based on a number of factors generally accepted as important in evaluating the adverse effects on product quality and consumer health. It is intended as a guide in determining what level of testing, if any, is necessary to assure the quality of the product. Conducting a microbiological risk assessment involves professional judgment and/or a microbiological analysis, if necessary, to determine the level of risk.

The nature and frequency of testing vary according to the product. The significance of microorganisms in non-sterile cosmetic products should be evaluated in terms of the use of the product, the nature of the product and the potential harm to the user.

The degree of risk depends on the ability of a product to support the growth of microorganisms and on the probability that those microorganisms can cause harm to the user. Many cosmetic products provide optimum conditions for microbial growth, including water, nutrients, pH and other growth factors. In addition, the ambient temperatures and relative humidity at which many cosmetic products are manufactured, stored and used by consumers, will promote growth of mesophiles that could cause harm to users or cause degradation of the product. For these types of product, the quality of the finished goods is controlled by applying cosmetic good manufacturing practices (GMPs) (see ISO 22716) during the manufacturing process, using preservatives and conducting control tests using appropriate methods.

The likelihood of microbiological contamination for some cosmetic products is extremely low (or non-existent) due to product characteristics that create a hostile environment for survival/growth of microorganisms. These characteristics are elaborated in this International Standard. While the hazard (adverse effects on product quality and consumer health) may remain the same for these products, the likelihood of an occurrence is extremely low. Those products identified as “hostile” and produced in compliance with GMPs pose a very low overall risk to the user.

Therefore, products that comply with the characteristics outlined in this International Standard do not require routine microbiological testing.

The objective of these guidelines is to help cosmetic manufacturers and regulatory bodies to determine when, based on a “risk assessment,” the routine application of the microbiological International Standards for cosmetics and other relevant methods is not necessary.

Cosmetics — Microbiology — Guidelines for the risk assessment and identification of microbiologically low-risk products

1 Scope

The objective of this International Standard is to help cosmetic manufacturers and regulatory bodies define those finished products that, based on a risk assessment, present a low risk of microbial contamination during production and/or use, and therefore, do not require the application of microbiological International Standards for cosmetics.

2 Terms and definitions

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

2.1
risk
effect of uncertainty on objectives

[ISO Guide 73:2009, definition 1.1]

NOTE Microbiological risk is associated with the ability of a product to:

— support the growth of microorganisms and the probability that those microorganisms can cause harm to the user;

— support the presence of specified microorganisms as identified in cosmetic microbiological International Standards, e.g. ISO 18415, ISO 18416, ISO 22717, ISO 22718 and ISO 21150.

2.2
risk assessment
overall process of risk identification, **risk analysis** (2.3) and **risk evaluation** (2.4)

[ISO Guide 73:2009, definition 3.4.1]

2.3
risk analysis
process to comprehend the nature of **risk** (2.1) and to determine the level of risk

[ISO Guide 73:2009, definition 3.6.1]

2.4
risk evaluation
process of comparing the results of **risk analysis** (2.3) with **risk criteria** (2.5) to determine whether the **risk** (2.1) and/or its magnitude is acceptable or tolerable

[ISO Guide 73:2009, definition 3.7.1]

where

p is the vapour pressure of the solution;

p_0 is the vapour pressure of pure water;

n_1 is the number of moles of solute;

n_2 is the number of moles of water.

When a solution becomes more concentrated, vapour pressure decreases, and the water activity falls from a maximum of 1,00 (a_w for pure water). These conditions have been categorized with respect to their capacity to grow and produce metabolites in various conditions and values of a_w. The influence of reduced a_w on microorganisms is well documented. As the amount of free water in a formulation is reduced (decrease in a_w), the microorganism is faced with the challenge of maintaining a state of turgor within the cell. Loss of turgor will result in slower growth and eventually death of the cell. Many organisms survive under conditions of low a_w but will not grow. Lowered a_w causes an increase in the lag phase of growth, decrease in growth and decrease in total cell count. At very low values of a_w, it can be assumed that the lag phase becomes infinite, i.e. no growth. In low a_w environments, cells shall use energy to accumulate compatible solutes to maintain internal pressure. The growth of most bacteria is confined to an a_w above 0,90. Yeast and mould can grow at a much lower a_w with a limiting value above 0,60. See reference [1].

Listed below are examples of the minimum water activity levels required for growth of selected microorganisms.

Table 1 — Approximate minimum water activity, a_w, required for growth of selected microorganisms
(see reference [2])

Microorganism	a_w
Most bacteria	0,90
Pseudomonas species	0,96
Enterobacteriacae	0,93
Staphylococcus aureus	0,86
Most spoilage yeast	0,70
Most spoilage mould	0,60

The above water activity values should be considered as reference points, since microbial growth may occur at lower values depending on differences in temperature, pH or nutrient content of the product formulation. Even though water activity values are important in assisting in the risk analysis for microbial contamination, water activity should not be used as the sole indicator in determining whether product testing is necessary for a particular product formulation. Other factors such as manufacturing and filling temperatures should be taken into consideration to determine if a product requires further microbiological testing.

3.2.3 pH of formulation

The use of acidic pH is a common practice in the food industry for protection against bacteria and these same principles apply to cosmetics. The combination of acidic pH and a_w has been thoroughly studied (see reference [3]). In many instances, the level of inhibition on microbial activity depends on the specific acid being used. Acidic conditions around pH 5 favour mould and yeast proliferation but will not support bacterial growth. As the pH falls below pH 3,0, the conditions for growth of yeast become hostile (see reference [4]); this is because intercellular pH has to be maintained within relatively narrow limits.

Alkaline pH may also create a hostile environment and may in some products be used as part of their preservative system. Liquid soaps with alkaline pH (pH 9,0 to pH 10,0) present an environment unfavourable for the growth of some microorganisms (see reference [5]). Hair curl relaxers, due to their extreme pH (around 12), prevent the growth of virtually all microorganisms that would be likely to contaminate cosmetic products (see reference [6]).

The reason for this is that the extreme pH, either acidic or alkaline, makes it necessary for microorganisms to expend energy on maintenance of intercellular pH rather than growth. When pH is used in combination with chelating agents, glycols, anti-oxidants, water activity and high surfactant levels, an environment can be created which will not support microbial growth.

These concepts may be visualized as “hurdles” that microorganisms must overcome in order to grow (see reference [7]).

In certain product types, where extreme pH levels are reported, those considered above pH 10,0 and below pH 3,0 do not require microbiological testing, including both challenge-test and end product testing. At all other pH values ($3{,}0 \leqslant \text{pH} \leqslant 10{,}0$) a combination of pH and other physico-chemical factors needs to be evaluated to determine potential risk. Data to support the conclusion that the microbiological risk is low may need to be generated, either through experimental design or review of product history.

3.2.4 Alcohol content

Microbial growth is prevented in aqueous systems containing > 20 % by volume mass of absolute ethyl alcohol. However, lower alcohol levels (5 % to 10 %) may have additive or synergistic activity when combined with other physico-chemical factors (see reference [8]).

Ethanol, *n*-propanol and *iso*-propanol are the most frequently used aliphatic alcohols in cosmetic preparations (see reference [9]). Their antimicrobial efficacy increases with molecular weight and chain length. The concentration in which they are present in a product determines whether they will kill or merely inhibit microorganisms. Data in the literature indicate that the microbiostatic effect of alcohol is quite high in the range of 10 % to 20 %, and will allow for a reduction in preservation. Depending on the pH of the substrate, 15 % to 18 % ethyl alcohol has generally been considered acceptable for preservation (see reference [10]).

Products containing alcohol levels > 20 % by volume mass do not require microbiological testing (challenge-test and end product testing). At levels below 20 %, other physico-chemical factors need to be evaluated to determine potential risk. Data to support the conclusion that the microbiological risk is low may need to be generated, either through experimental design or review of product history.

3.2.5 Raw materials that can create a hostile environment

The use of certain raw materials in cosmetic formulations will help to create an environment that is hostile to microbial growth. Data to support the conclusion that microbial growth has been inhibited may need to be generated, either through literature reference, experimental design or review of product history. The following are examples of some materials that create such an environment.

a) Strong oxidising agents (e.g. hydrogen peroxide) (see reference [11]), or strong reducing agents (e.g. thiol compounds).

b) Polar organic solvents (e.g. ethyl acetate).

c) Oxidising dyes.

d) Aluminium chlorohydrate and related salts.

The use of high levels of aluminium chlorohydrate ($\geqslant 25$ %) in certain deodorants and anti-perspirants gives rise to an acidic pH and a low a_{W} value, making these products intrinsically hostile to microbial growth (see reference [12]). In these conditions, the microbiological risk can be considered to be controlled and these products do not require microbiological testing (challenge-test and end product testing).

e) Propellant gases.

In the case of cosmetics where a propellant gas (e.g. dimethyl ether, isobutane) is used to help deliver the product, (hairsprays, deodorants, shaving foam, etc.), microbial growth is hindered by the fall in the partial pressure of oxygen, and in certain cases by the intrinsic inhibiting effect of the propellant gas (see references [13][14][15][16][17]).

f) Other substances.

Other raw materials can be hostile to microbial growth. Data to support the conclusion that the microbiological risk is low may need to be generated, either through literature reference, experimental design or review of product history.

3.3 Production conditions

Certain aspects of the manufacturing and filling process (e.g. high temperature) may reduce the microbiological risk to a cosmetic product. As with pH, there is an optimum temperature range for microbial growth. Low temperatures will allow for slow growth and raising temperatures could potentially increase growth. As the temperature rises above optimum, growth is inhibited and microorganisms are killed. Heat is used to control microorganisms either by applying a temperature adequate for rapid kill or by maintaining a temperature above optimum for an extended period of time (see reference [18]).

A temperature above 65 °C can cause thermal inactivation of the microbial bioburden in a product formulation. With a 10 min hold time at a temperature of 65 °C, most vegetative bacterial cells die due to degradation of cellular proteins.

Based on the above information, microbial content testing on product formulations that are filled at a temperature above 65 °C is not required. Periodic testing of the product or verification of the lethality of the process temperature should be considered. It is also recommended that periodic review of manufacturing and filling be performed to ensure there have been no changes to the conditions of the process.

3.4 Packaging

The type of packaging components chosen for the presentation of a cosmetic product has a direct influence on the risk of its contamination in use (see reference [19]) and shall be taken into account in the microbiological risk evaluation during use.

— Certain packaging components give physical protection against contamination from consumer use (e.g. a pump dispenser, single dose units) and contribute to the protection and preservation of a formulation.

— Other factors such as a small product volume limiting the number of uses or an indication of short duration of use also contribute to the protection of formulation.

— Certain presentations, e.g. pressurized delivery (see 3.2.5) or unit-dose, provide full protection of the cosmetic formulation from contamination during use. If the product is microbiologically acceptable when marketed, it will remain so throughout its use. In this case, the microbiological risk during use is low, based on the high level of protection provided by the package.

3.5 Combined factors

Combinations of the factors mentioned in this International Standard can create an environment that is hostile to microbial growth or survival. These combined factors should be taken into account when determining if a product is subject to the appropriate microbiological standards regarding testing and/or product stability (see reference [20]).

The exemption from testing should be based on appropriate justification. This determination is the responsibility of the manufacturer. Data to support the conclusion that the microbiological risk is low may need to be generated, either through literature reference, experimental design or review of product history.

4 Identified low-risk products

After review of 3.1 to 3.5, products that meet any of the following product characteristics and their combinations may be considered as examples of low-risk products.

Table 2 — Examples of low-risk products

Physico-chemical factor	Limit	Example
pH	$\leqslant$ 3,0	Skin peels (glycolic acid)
pH	$\geqslant$ 10,0	Hair relaxers
Ethanol or other alcohol	$\geqslant$ 20 %	Hair sprays, tonics, perfumes
Filling temperature	$\geqslant$ 65,0 °C	Lip balms, lipsticks, cream blushes
Water activity (a_w)	$\leqslant$ 0,75[a]	
Solvent-based products		Nail enamels
Oxidizing products		Hair dyes
Aluminium chlorohydrate	$\geqslant$ 25 %	Anti-perspirants
[a] See reference [21].		

Bibliography

[1] SILLIKIER, J.H. et al., eds. for the International Commission on Microbiological Specifications for Food, *Microbiology Ecology of Foods*, **1**, Academic Press, Orlando, Fl, pp. 76-91, 1980

[2] CURRY, J., Water Activity and Preservation, *Cosmetic and Toiletries*, **100**, pp. 535-54, 1985

[3] TROLLER, A., Effects of a_w and pH on growth and survival of Staphylococcus aureus. In: *Properties of Water in Foods*, STIMATOS, D. and MULTON, J.L., eds., Martinus Nijhoff, Dordecht, 1985

[4] PITT, J.I., Resistance of some food spoilage yeasts to preservatives, *Food Technology*, **26**(6), pp. 238, 239, 241, 1975

[5] KABARA, J.J. and ORTH, D., *Preservative Free and Self Preserving Cosmetics and Drugs*, Marcel Dekker, pp. 1-14, 1997

[6] OBUKKOWHO, P. and BIRMAN, M., Hair curl relaxers, *Cosmetic and Toiletries*,**107** (12), pp. 39-43, 1992

[7] LEISTNER, L., Hurdle technology applied to meat products of the shelf stable product and intermediate moisture types. In: *Properties of Waters in Foods*, SIMATOS, D. and MULTON, J.L., eds., Martinus Nijhoff, Dordecht, 1985

[8] KABARA, J.J. and ORTH, D.S., *Principles for product preservation in preservative-free and self-preserving cosmetics and drugs*, Marcel Dekker, New York, p. 248, 1997

[9] BANDELIN, F.J., Antibacterial and preservative properties of alcohols, *Cosmetic and Toiletries*, **92**, pp. 59-70,1977

[10] BLOCK, S., *Disinfection, Sterilization and Preservation*, 4th Edition, Lea & Febiger, pp. 892, 1991

[11] BLOCK, S., *Disinfection, Sterilization and Preservation*, 4th Edition, Lea & Febiger, pp. 167-172, 1991

[12] KABARA, J.J. and ORTH, D.S., *Principles for product preservation in preservative-free and self-preserving cosmetics and drugs,* Marcel Dekker, New York, pp. 1-14, 1997

[13] IBRAHIM, Y.K.E. and SONNAG, H.G., Preservative potentials of some aerosol propellants — Effectiveness in some pharmaceuticals, *Drugs made in Germany*, **2**, 1995

[14] IBRAHIM, Y.K.E, GEISS, H.K. and SONNAG, H.G., Alternatives to traditional preservatives, *SOFW Journal*, **118**, Jahrgang 6/92

[15] Commission SFSTP, DECLERCK, J., CAIRE-MAURISIER, F., GENOT, P., LEVACHER, E., MICHAUT, A., SCHEIBER, G. and Tardivet, S. Les gaz propulseurs: Les HFC (hydrofluorocarbones) alternatives aux CFC, *Pharmapratiques*, **16**, No. 1, pp. 61-72, 2006

[16] MEIER, M., FISHER, F.X., KELLER, M. and HALFMANN, H.-J., Influence of alternative propellants on microbial viability in comparison to chlorofluorocarbons, *Pharm. Ind*., **58**, pp. 78-82

[17] SAWYER, E., GREEN, B. and COLTON, H., Micro-organisms survival in non-CFC propellants P11 and P12, *Pharmaceutical Technology*, pp. 90-96, 2001

[18] *Microbial Ecology of Foods — Factors Affecting Life and Death of Microorganisms*, International Commission on Microbiological Specifications for Foods, Academic Press, pp. 16-19, 1980

[19] BRANNAN, D.K. and DILLE, J.C., Type of closure prevents microbial contamination of cosmetics during consumer use, *Appl. Environ. Microbiol*., **56**, pp. 1476-1479, 1990

[20] *Recommendations Relating to Period After Opening (P.A.O) Assessment* — Division for the Evaluation of Advertising, Cosmetics, and Biocides: European Commission (04/ENT/COS/28) March 11, 2005

Water activity

[21] US Pharmocopeia, chapter 1112 — *Application of Water Activity Determination to Non-sterile Pharmaceutical Products*, 2007

[22] SCOTT, W.J., Water relations of Staphyloccocus aureus at 30 °C, *Austral. J. Biol. Sci.*, **6**, p. 549, 1953

[23] SERBER, W.H., Influence of water activity on foodborne bacteria: a review, *J. Food Protect.*, **46**(2), pp. 142-150, 1983

[24] FRIEDEL, R.R., The Application of Water Activity Measurement to Microbiological Attributes Testing of Raw Materials Used in the Manufacture of Non-Sterile Pharmaceutical Products, *Pharmacopeial Forum*, **25**(5), pp. 8974-8981, 1999

[25] ENIGL, D.C., Creating Natural Preservative Systems by Controlling Water Activity, *Pharmaceutical Formulation & Quality*, **29**-**30**, 1999

[26] ENIGL, D.C. and SORRELS, K., *Preservative-Free and Self-Preserving Cosmetics and Drugs Principles and Practice*, Marcel Dekker, Chapter 3 *Water Activity and Self-Preserving Formulas*, pp. 45-73, 1997

See also reference [2].

pH

[27] *Food Preservatives*, 2nd Edition, RUSSEL, N.J. and GOULD, G.W. eds, Kluwer Academic/Plenum Publishers, pp. 25-42, 2003

[28] SILLIKER, J.H. et al. eds. for the International Commission on Microbiological Specifications for Food, *Microbial Ecology of Foods*, **1**, Academic Press, Orlando, FL, pp. 92-111, 1980

[29] *Cosmetic Microbiology, A Practical Handbook*, BRANNAN, D., ed., CRC Press, pp. 47-49, 1991

High temperature

[30] International Dairy Foods Association http://www.idfa.org/facts/milk/pasteur.cfm

[31] *Microbial Ecology of Foods — Factors Affecting Life and Death of Microorganisms*, International Commission on Microbiological Specifications for Foods, Academic Press, pp 16-37, 1980

Oxidizing agents

[32] HARRISON, S. and SINCLAIR, R., Hair Coloring, Permanent Styling and Hair Structure, *Journal of Cosmetic Dermatology*, **2**, p. 180, 2003

See also reference [6].

Packaging/Closures

[33] BRANNAN, D.K., Packaging's Role in Preservation, *Cosmetics and Toiletries*, **113,** 1998

See also references [12] [19].

Propellents

[34] IBRAHIM, Y.K. and SONNTAG, H.G., Effect of formulation pH and storage temperatures on the preservative efficacy of some gases used as propellants in cosmetic aerosols, *J. Appl. Bacteriol.*, **74**, p. 20, 1993

[35] KLEPAK, P.B. In Vitro Killing Time Studies of Antiperspirant Salts, *Z. Aerosol. Parf. Seifen Ole Fette Wachse*, **13**, p. 478, 1990

See also references [13] [14] [15] [16] [17].

Alcohols

[36] PINON, A. et al., Growth, survival and inactivation of Pseudomonas aeruginosa and Staphylococcus aureus strains of various origin in the presence of ethanol, *International Journal of Cosmetic Science*, **29**, pp. 111-119, 2007

[37] *Cosmetic Microbiology, A Practical Handbook*, BRANNAN, D., ed., CRC Press, pp. 167-168, 1991

[38] BAIRD and BLOOMFIELD, eds., *Microbial Quality Assurance in Cosmetics, Toiletries and Non-Sterile Pharmaceuticals*, 2nd Edition, Taylor and Francis Ltd., London 1996

Risk assessment/Statistics

[39] Managing Quality Risk Management Implementation, *PDA Letters*, **18**, pp. 1-13, 2007

[40] COLEMAN, M.E. et al., Microbial Risk Assessment Scenarios, Causality and Uncertainty, *Microbe*, **2**, pp. 13-17, 2007

[41] DURKEE, J., It's a Two-edged Sword, The Magnificent 7 Controlled Environments, **10**, p. 34, 2007

[42] DURKEE, J., The “Magnificent Seven” — Part II. *Controlled Environments*, **10**, p. 28, 2007

[43] COHEN, N., The Use of Exponentially Weighted Process Statistics (EWPS) and Statistical Process Control (SPC) in High Frequency Data Acquisition of Pharmaceutical Water Systems Instrumentation, *Pharm Eng*. **27**, pp. 72-82, 2007

[44] KÖPPEL, H., SCHNEIDER B. et al., Out-of Specification Test Results from the Statistical Point of View, *J Pharmacol and Biomedical Analysis*, **44**, pp. 718-729, 2007

[45] LIU, Y., Overview of Some Theoretical Approaches for Derivation of the Monod Equation, *Appl. Microbiol Biotechnol*., **73**, pp. 1241-1250, 2007

[46] MCCLURE, F. and LEE, J., Exact One-Tailed 100% Upper Limits for Future Sample Repeatability Relative Standard Deviations Obtained in Single and Multilaboratory Repeatability Studies, *J AOAC International*., **90**, pp. 1701-1705, 2007

[47] Microbiological Risk Factor Assessment of Atypical Cosmetic Products, *CTFA Microbiology Guidelines*, Cosmetic Toiletry and Fragrance Association, 2007

[48] Method for Preservation Testing of Atypical Cosmetic Products, *CTFA Microbiology Guidelines*, Cosmetic Toiletry and Fragrance Association, 2007

[49] International Conference on Harmonization, Q6A — Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products Decision Tree 6, 1999

[50] Principles and Guidelines for the Conduct of Microbiological Risk Assessment CAG/GL 30, 1999

International Standards

[51] ISO Guide 73, *Risk management — Vocabulary*

[52] ISO 18415, *Cosmetics — Microbiology — Detection of specified and non-specified microorganisms*

[53] ISO 18416, *Cosmetics — Microbiology — Detection of Candida albicans*

[54] ISO 21150, *Cosmetics — Microbiology — Detection of Escherichia coli*

[55] ISO 22716, *Cosmetics — Good Manufacturing Practices (GMP) — Guidelines on Good Manufacturing Practices*

[56] ISO 22717, *Cosmetics — Microbiology — Detection of Pseudomonas aeruginosa*

[57] ISO 22718, *Cosmetics — Microbiology — Detection of Staphylococcus aureus*

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Egne notater/Notes:

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