SLOVENSKI STANDARD
SIST-TP ISO/TR 14735:2013

01-november-2013

Kozmetika - Analizne metode - Nitrozamini: tehnično navodilo za zmanjševanje in določevanje N-nitrozaminov v kozmetiki

Cosmetics - Analytical methods - Nitrosamines: Technical guidance document for minimizing and determining N-nitrosamines in cosmetics

Cosmétiques - Méthodes analytiques - Nitrosamines: Directives techniques concernant la limitation et le dosage des N-nitrosamines dans les produits cosmétiques

Ta slovenski standard je istoveten z: ISO/TR 14735:2013

ICS:

71.100.70	Kozmetika. Toaletni pripomočki	Cosmetics. Toiletries

SIST-TP ISO/TR 14735:2013 **en**

TECHNICAL REPORT

ISO/TR 14735

First edition
2013-04-15

Cosmetics — Analytical methods — Nitrosamines: Technical guidance document for minimizing and determining N-nitrosamines in cosmetics

Cosmétiques — Méthodes analytiques — Nitrosamines: Directives techniques concernant la limitation et le dosage des N-nitrosamines dans les produits cosmétiques

Reference number
ISO/TR 14735:2013(E)

COPYRIGHT PROTECTED DOCUMENT

ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web www.iso.org

Published in Switzerland

Contents

Page

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. 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. 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.

The committee responsible for this document is ISO/TC 217, *Cosmetics*.

Introduction

N-nitrosamines are a class of compounds that have been known for over 100 years. The carcinogenicity of N-nitrosamines has been well studied and of the compounds tested, approximately 90 % have been shown to be carcinogenic across a number of animal species (Magee et al. 1976). As a result of these findings, N-nitrosamines are considered to be carcinogenic to humans (IARC 1978) and minimization of exposure to N-nitrosamines is recognized as important to the preservation of human health. N-nitrosamines are formed by the reaction of secondary amino compounds with nitrosating agents such as nitrite or oxides of nitrogen (Ikeda Challis et al. 1977, Ikeda et al. 1990). Traces of N-nitrosamine in cosmetics may result through the use of certain cosmetic ingredients and/or through the nitrosation of the precursors principally secondary amines present in finished cosmetic products (Harvey et al. 1994).

In cosmetics, secondary dialkanolamines are used in the production of dialkanolamides and secondary dialkylamines are used in the production of dialkylamides. In the presence of nitrogen oxides present as impurities or produced from other cosmetic ingredients, nitrosation of secondary amine may occur, resulting in the formation of the N-nitrosamine. Similarly, the presence of secondary amines in trialkylamines and trialkanolamines may result in the formation of N-nitrosamines following nitrosation with nitrogen oxides (SCCS/1458/11). N-nitrosamines may also be formed from nitro substituted para aminophenols in the presence of a secondary amino compound.

Concerns about N-nitrosamine contamination of cosmetics date back to at least 1979 (United States Federal Register Notice, 44 FR 21365, April 10, 1979). Although the potential for N-nitrosodiethanolamine (NDELA) contamination of cosmetic products and ingredients still exists, in principle, coordinated efforts between regulators and the regulated industry since 1979 has successfully addressed the detection, inhibition, decomposition, and prevention of NDELA formation, and resulted in a several references in the literature on analytical technical methods and formulation guidance for avoidance of the formation of NDELA and other N-nitrosamines. (US FDA Guide To Inspections Of Cosmetic Product Manufacturers). Further, vigilant testing programs by industry and inspection programs by regulators to assess their ingredients and cosmetic products for NDELA and other N-nitrosamines have demonstrated the effectiveness and have greatly reduced cosmetics as a major source of N-nitrosamine exposure to consumers.

N-nitrosamines are also covered in European cosmetics regulation. The Fifteenth European Commission Directive 92/86/EEC relating to cosmetic products does not allow the marketing of cosmetic products that contain nitrosamines. The presence of trace levels in cosmetic products is allowed, if they are technically unavoidable, as long as the product does not cause damage to human health when applied under normal or reasonably foreseeable conditions of use. This requires N-nitrosamine levels to be kept as low as reasonably practicable, although no specific level has been set for finished cosmetic products. This Directive also set a limit of 50 µg kg $^{-1}$ (ppb) for the N-nitrosodialkanolamine content of fatty-acid dialkanolamides, monoalkanolamines and trialkanolamines used as raw materials in the manufacture of cosmetic products. A similar limit 50 µg kg $^{-1}$ has been set for the N-nitrosodialkylamine content of fatty-acid dialkylamides, monoalkylamines and trialkayamines and their salts because the properties of these compounds are similar to their respective alkanolamine analogues with respect to their potential as precursors of N-nitrosamine formation (European Commission Directive 2003/83/EC).

In order to demonstrate compliance with regulatory requirements and to allow reliable risk assessments to be performed, relevant application of appropriate analytical methods is required. A range of methods for N-nitrosamine determination are already available, two of which have become ISO Standards (ISO 15819, ISO 10130). It is important to understand the benefits and limitations of the analytical methods to provide appropriate data.

This guidance is mainly focused on the possible formation of N-nitrosamines and the analytical possibilities to detect their presence. It should be noted that the application of Good Manufacturing Practices (GMP) alone is not enough to prevent the presence of N-nitrosamines, hence this guidance also describes possible strategies for minimizing N-nitrosamine formation, methodologies available to measure N-nitrosamines and suggests a testing strategy which may be applied to both raw materials and finished products. Also included is some guidance on good analytical practice for each method, to ensure validity of the analytical data.

Cosmetics — Analytical methods — Nitrosamines: Technical guidance document for minimizing and determining N-nitrosamines in cosmetics

1 Scope

This Technical Report aims to contribute to providing general advice on strategies that can be adopted to minimize the likelihood of N-nitrosamine formation in cosmetic products and provide a description of the analytical methodologies available for the reliable determination of N-nitrosamines in cosmetic products. It also seeks to provide some insight into the relevance and limitations of each of the methods described and finally provide an analytical approach for the analysis of N-nitrosamines in cosmetic products and raw materials.

This Technical Report covers the reduction or elimination of adventitious nitrite sources, reduction or elimination of secondary amino sources, incorporation of inhibitors to N-nitrosamine formation and analytical methodologies for total N-nitroso compounds and specific methods for N-nitrosodiethanolamine (NDELA).

2 N-nitrosamine chemistry

N-nitroso compounds are characterized by a nitrosyl group (-*N* = O) bonded to a nitrogen atom, but may also contain a number of other functional groups. The N-nitrosamines are composed of the dialkyl, alkylaryl, and cyclic nitrosamine derivatives. Conditions for the formation of N-nitroso compounds can occur in a number of situations. Theoretically, N-nitroso derivatives can be formed whenever any compound containing a secondary amino group comes into contact with an active nitrosating agent (see SCCS/1458/11).

3 Minimization strategies

3.1 Reduction or elimination of adventitious nitrite sources

In line with Good Manufacturing Practices, the level of adventitious nitrite can be minimized by using purified water in manufacture and the use of nitrite-free steel or plastic containers for storage of raw materials and products. It is also important to minimize contact with air containing oxides of nitrogen during the product manufacturing process, separating production from hydrocarbon fuel equipment and open flames (e.g. using indirect heating systems). Eliminating unnecessary nitrates or nitrites from raw materials (e.g. minimizing use of raw materials manufactured in the presence of oxides of nitrogen) is essential in minimizing adventitious nitrite.

Under certain circumstances, if traces of secondary amines are present, they may be nitrosated. It should be noted that some preservatives may catalyse potential nitrosating reactions. The advice of the preservative manufacturer should be sought, if there is uncertainty about the potential for nitrosation to occur in a product.

It is important to check if specific restrictions exist in cosmetics legislation, i.e. national or regional, regarding the combination of an ingredient with a nitrosating agent. For example, in Europe, the European Cosmetics Regulation imposes a specific restriction on the use of sodium nitrite. Sodium nitrite must not be used with secondary and/or tertiary amines or other substances forming N-nitrosamines (Colipa 2009).