Cosmetics Europe
the personal care association

ARGUMENTATION PAPER: HOW INDUSTRY MINIMIZES THE UNWANTED PRESENCE OF N-NITROSAMINES IN COSMETICS FINISHED PRODUCTS –

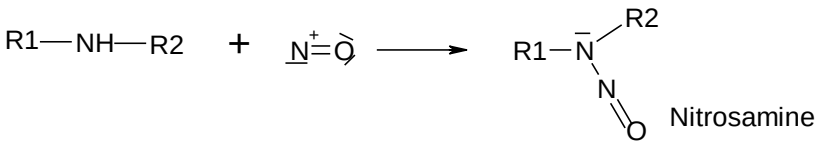
Scope:

This document summarizes the strategy implemented by the cosmetic industry to minimize as low as it is reasonably achievable the presence of N-nitrosamine as unintended traces of contaminant in the cosmetics finished product.

Background:

Nitrosamines are chemical substances identified since 1976. Some of nitrosamines, such as N-nitrosodiethanolamine (NDELA) and N-nitrosodimethylamine (NDMA) are classified as category 1B carcinogens.
Annex II entry No. 410 of the Regulation (EC) No. 1223/2009 (hereafter "CPR") states that Nitrosamines must not form part of the composition of cosmetic products. However, according to Article 17 (Traces of prohibited substances) of the CPR, they are accepted as traces that are technically unavoidable in Good Manufacturing Practice, as long as the finished product conforms with Article 3 of the CPR (it does not cause damage to human health when applied under normal or reasonably foreseeable conditions of use).
Nitrosamines may be present as contaminants in a number of consumer products including food (such as certain beverages), tobacco products (one of the main source of pre-formed nitrosamines), rubber products and also cosmetics.
Cosmetics Europe has therefore issued in 2009 a "Technical Guidance Document on minimizing and determining Nitrosamines in Cosmetics".

Formation of N-nitrosamines:
N-Nitroso compounds contain a nitrosyl group (-N=O) bonded to a nitrogen atom, and may contain other functional group of course (dialkyl, alkylaryl and cyclic nitrosamine derivatives).
Main formation of relevant nitrosamines can occur by the reaction of amino compounds with nitrosating agents.



Nitrogen oxide may refer to a mixture of compounds and could come from different sources (Air, RM…), This reaction can be produced also under neutral pH during the manufacture and/or the storage of a raw material or in-situ in formula. Different compounds could catalyze or inhibit this reaction

According to the recommendation of the Scientific Committee on Consumer Safety (SCCS) the regulatory authorities imposed a number of strict measures intended to limit the formation of nitrosamines in cosmetic products, resulting in a very low level of N-nitroso compounds.

Nevertheless, nitrosamines potentially present in cosmetic products at safe trace levels remains a frequent target of concern although their presence is minimized and doesn't present a risk for human health.

Regulatory provisions set by the CPR:

- Prohibited ingredients:
  - Nitrosamines e.g. Dimethylnitrosoamine; Nitrosodipropylamine; 2,2'-Nitrosoimino)bisethanol (II/410)
  - Secondary alkyl- and alkanolamines and their salts (II/411)

However, according to CPR Article 17 "Traces of prohibited substances" they are accepted as traces that are technically unavoidable in Good Manufacturing Practice and provided the Cosmetic Products are safe.

- Restriction of nitrosating agents:
  - Sodium nitrite is limited to 0.2% max in the finished product as a rust inhibitor with a requirement not to use with secondary and/or tertiary amines or other substances forming nitrosamines (III/17).
  - Preservatives 5-bromo-5-nitro-1.3-dioxane and bronopol (2-bromo-2-nitropropane-1.3-diol) with the requirement not to exceed 0.1% max in the finished product and to avoid formation of nitrosamines (VI /20 and 21),

Substances subject to specific restrictions: e.g. minimum purity, maximum secondary amine content, maximum nitrosamine content, storage in nitrite-free containers, use levels and avoidance of nitrosating systems.

- Dialkylamides, dialkanolamides of fatty acids (III/60)- example Cocamide DEA, DEA Lauryl sulfate
- Monoalkanolamines, Monoalkylamines (III/61) example Ethanolamine
- Trialkylamines, trialkanolamines and their salts (III/62) example Triethanolamine

Strategy develop by the Industry to minimize nitrosamine formation as low as it is achievable.

1. **Prevention of formation of nitrosamines in cosmetic products:**
   Selection of suitable raw materials:
   - Require a high quality level of the raw materials (quality charter with suppliers and commitment)
   - avoid secondary dialkylamine or dialkanolamines and salts as ingredients

   Quality of raw materials
   - control the potential traces of secondary dialkylamine or dialkanolamines and salts, as impurity coming from others raw materials, in order to avoid unwanted nitrosation reaction,
   - consider and detect traces of secondary amine (DEA, cocamide DEA, DPPA)

   Respect the formulation rules:
   - Avoid any combination of ingredient nitrosating agent/nitrosable agent, ()
   - Introduce an anti-nitrosating agent
   - Introduce an inhibitory system of nitrosamine formation in the case of formulas containing: The efficacy of any potential inhibitor must be established for each individual application (Inhibitors system are described in the literature)
     • Inhibitors soluble in water: ascorbic acid…
     • Inhibitors soluble in oil: ascorbyl palmitate, tocopherol…
     • Inhibitors soluble in water/oil: gallic acid
   - Reduce emulsion systems based on amines

2. **Manufacturing process according to GMPs**
   During the production, the level of accidental nitrite can be minimized thanks to the use of purified water, nitrite-free steel containers, plastic containers, and any measures to avoid nitrite traces.

3. **Perform regular evaluation on NDELA presence over time and implement an analytical control plan:**
   - Traceability in raw material considered at risk and in finished products
   - Technical knowledge acquirement and adaptation into formulas

For the general management of N-nitrosamines, the application of the flowchart developed at ISO level in the technical guidance for minimizing and determining N-nitrosamine in cosmetics is 14735:2013 is recommended to apply.

References:

- Safety assessment: SCCS/1486/12 Final; SCCS/1458/11 Final;
- European cosmetic product regulation 1223/2009 (EC);
- Cosmetics Europe- "Technical Guidance Document on minimizing and determining Nitrosamines in Cosmetics", 2009;
- ISO/TR 14735:2013 - Cosmetics - Analytical methods -Nitrosamines: Technical guidance document for minimizing and determining Nnitrosamines in cosmetics;