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REGULATORNI ASPEKTI PREPARATA ZA ISPIRANJE USTA: SLUČAJ REPUBLIKE SEVERNE MAKEDONIJE

REGULATORY ASPECTS OF MOUTHWASHES: THE CASE OF REPUBLIC OF NORTH MACEDONIA

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Sažetak

Uvod: *S obzirom na to rastvori za ispiranje usta mogu izazvati neželjene efekte, pacijenti i zdravstveni radnici treba da prijave neželjene događaje nacionalnim institucijama. Da bi se osigurala bezbednost ovih proizvoda i olakšalo prijavljivanje neželjenih događaja, neophodno je da pacijenti i zdravstveni radnici budu svesni regulatornog statusa proizvoda koji je odgovoran za neželjeni događaj.*
Cilj *ovog rada bio je da se ispita regulatorni status preparata za ispiranje usta dostupnih na tržištu u Republici Severnoj Makedoniji.*
Materijali i metode*: Istraživanje tržišta je sprovedeno u Republici Severnoj Makedoniji, pokrivajući i tradicionalna i onlajn tržišta. Preparati za ispiranje usta su kupljeni direktno od prodavaca, Imena robnih marki proizvoda i regulatorne informacije naznačene na njihovoj ambalaži su dokumentovane.*
Rezultati: *U vreme sprovođenja ovog istraživanja na tržištu Republike Severne Makedonije bilo je dostupno ukupno 76 preparat za ispiranje usta. Većina njih (n=71, 93,43%) je klasifikovana kao kozmetički proizvodi, dok su 3 (3,94%) kategorisani kao lekovi, a 2 (2,63%) kao medicinski proizvodi. Utvrđena je statistički značajna razlika između broja preparata za ispiranje usta klasifikovanih kao kozmetički proizvodi i onih registrovanih kao lekovi ili medicinski uređaji.*
Zaključak: *Bez obzira na njihovu klasifikaciju, sve preparate za ispiranje usta moraju biti u skladu sa nacionalnim i međunarodnim bezbednosnim standardima pre stavljanja na tržište i moraju biti podvrgnute budnosti nakon stavljanja na tržište tokom normalne ili razumno predvidive upotrebe.*

Ključne reči: *preparati za ispiranje usta, regulacija, medicinski uređaji, kozmetika, bezbednost*

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Abstract

Background: *Considering that mouthwashes can cause side effects, patients and healthcare professionals should report adverse events to national authorities. To ensure the safety of these products and facilitate the reporting of adverse events, it is essential for patients and healthcare professionals to be aware of the regulatory status of the product responsible for the undesirable event.*
The aim *of this paper was to examine the regulatory status of mouthwashes available on the market in the Republic of North Macedonia.*
Materials and Methods: *A market survey was conducted in the Republic of North Macedonia, covering both traditional and online markets. Mouthwashes were purchased directly from vendors. The brand names of the products and the regulatory information indicated on their packaging were documented.*
Results: *A total of 76 mouthwashes were available on the market in the Republic of North Macedonia at the time of conduction of this research. Most of these (n=71, 93.43%) were classified as cosmetic products, while 3 (3.94%) were categorized as medicines, and 2 (2.63%) as medical devices. A statistically significant difference was found between the number of mouthwashes classified as cosmetic products and those registered as medicines or medical devices.*
Conclusion: *Regardless of their classification, all mouthwashes must comply with national and international safety standards prior to market placement and must be subject to post-market vigilance during normal or reasonably foreseeable use.*

Key words: *mouthwashes, regulation, medical devices, cosmetics, safety*

Introduction

Oral hygiene plays a crucial role in the prevention of many oral diseases, including periodontitis, tooth decay, and oral candidiasis. To prevent oral diseases, proper oral hygiene must be practiced ensuring the mouth, gums, and teeth are healthy[1]. Many scientific studies show a connection between oral health and cardiovascular diseases, diabetes, and even death[2,3]. To prevent caries formation and periodontal disease, effective oral hygiene should be performed, plaque should be removed and plaque formation should be prevented[4].

Throughout history, various products have been used to maintain oral hygiene. These include toothbrushes and toothpaste, mouthwashes, dental floss, miswak (chewing sticks), and toothpicks[5]. Patients and dentists are faced with different oral hygiene products. A consumer's choice regarding the appropriate product may be influenced by personal motives or advice from healthcare professionals, media advertisements, brand, the credibility of the company manufacturing the product, ingredients, availability of product information, and physical properties of products, such as their taste, flavor, color, and appearance, which are also influencing factors [6–10].

In the last few decades, mouthwashes and rinses have significantly expanded and developed as a category of oral care products [11]. A mouthwash is defined as a non-sterile aqueous solution used mostly for its deodorant, refreshing, or antiseptic effect. Mouthwashes or rinses are designed to reduce oral bacteria, remove food particles, temporarily reduce bad breath, and provide a pleasant taste[12].

The first known reference for using mouthwashes for the treatment of diseases of the gums is found in Chinese medicine, around 2700 BC[13]. The Egyptians were the first to put emphasis on a clean and healthy body and mixed water with honey to maintain good breath[14]. Later, in the Greek and Roman periods, mouth rinsing following mechanical cleaning became common among the upper classes, and Hippocrates recommended a mixture of salt, alum, and vinegar, while Pythagoras recognized the freshening effect of anise. Different products have been used for mouth rinsing over the centuries. In the 1500s, wine or beer was used; in the late 19th century, around 1890, the use of essential oils was introduced among dental care habits[15].

Today, on the market, there are numerous mouthwashes. There are many ingredients in mouthwashes, including oral health substances, solvents, surfactants and thickeners, sweeteners, plants (extracts, waters, and oils), preservatives, colorants, flavoring or cooling agents, and others. Some of the ingredients are not associated with medical benefits but are necessary for the creation of formulas, while some mouthwashes contain one or more active ingredients, like fluorine compounds, cetylpyridinium chloride, chlorhexidine, benzydamine hydrochloride, etc.[16,17]. The complex compounds of modern oral health products, including mouthwashes, make them one of the most sophisticated pharmaceutical products on the market today [11].

Mouthwashes can be used for therapeutic, diagnostic, and cosmetic purposes. Examples of therapeutic mouthwashes include allopurinol for treating stomatitis, pilocarpine for xerostomia, and nystatin for oral candidiasis. Toluidine blue mouth rinse is used as an adjunct tool for the detection of oral malignant and premalignant lesions[18]. Cosmetic mouthwashes (e.g., phenol and mint mouthwashes) may be used for refreshing purposes. Other topical mouthwashes include antiplaque (e.g., cetylpyridinium chloride) and fluorinated mouthwashes[19].

However, mouthwashes can be associated with undesirable effects or adverse events[20–22]. The most frequently reported adverse events were local morphological (oral mucosa and dental crown staining, mucosal lesions) and functional (taste modifications, abnormal oral sensation) alterations[22].

Considering that mouthwashes can cause side effects, patients or healthcare professionals must report adverse events to national authorities. To report adverse events and guarantee the safety of the products, it is necessary for patients and healthcare professionals to know the regulatory status of the product that caused the undesirable event, as well as the national competent authorities responsible for the vigilance of specific products. Specifically, depending on the regulatory status of the product, there are differences in terms of post-marketing surveillance of the products.

Aim

The aim of the paper was to examine the regulatory status of mouthwashes available on the market in the Republic of North Macedonia.

Materials and Methods

Between January 1, 2024, and July 1, 2024, market research was conducted in the Republic of North Macedonia. This research encompassed traditional markets (pharmacies, cosmetic chains, and consumer goods markets)

as well as the online market. Four researchers (VK, KI, SS, and BP) carried out this research aiming to identify all available mouthwashes. One to three packs of each mouthwash were purchased directly from vendors without requesting free samples from manufacturers or importers. Mouthwashes were selected based on the following inclusion criteria: intended for maintaining oral hygiene, preventing oral diseases, or having a therapeutic effect; available over-the-counter; and in the pharmaceutical forms of either a solution intended for direct use or a concentrate to be dissolved in water, regardless of their regulatory status (medicine, medical device, cosmetic product). The exclusion criteria included: tablets that dissolve in water or other liquids, chewing tablets, and saliva substitutes; products containing antibiotics, steroids, parasympathomimetic saliva stimulants, topical local anesthetics, and other prescription drugs; liquids taken orally but not intended for maintaining oral hygiene; liquids in the form of sprays, toothpastes, gels, powders, foams, homeopathic products, and products without a fully available composition.

Two researchers (VK and SS) recorded the brand names of the products and labeled the packaging information regarding regulatory status in an Excel spreadsheet. The authors considered national legislation related to the labeling of medicinal products, medical devices, and cosmetic products. Additionally, a review of the Register of Medicinal Products and Medical Devices maintained by the Agency for Medicines and Medical Devices of the Republic of North Macedonia (MALMED) was conducted. The other two authors (KI and BP) validated the data provided by VK and SS.

Frequency analysis of the regulatory status was performed using Microsoft Excel v. 2016 (Microsoft Corporation, Redmond, Washington, United States) and SPSS Statistics v. 23 for Windows (IBM Corp., Armonk, NY), while the difference between the proportions of means was analyzed using the Difference Test in StatSoft STATISTICA v. 12.5 (StatSoft, Inc., Tulsa, Oklahoma, United States).

Results

There were 76 mouthwashes available on the market in the Republic of North Macedonia at the time of the conduction of this research. A comprehensive list of these mouthwashes with their regulatory status is shown in Table 1:

Most of the available mouthwashes (n = 71, 93.43%) were cosmetic products, while 3 were classified as medicine (3.94%) and 2 as a medical device (2.63%) (Table 2).

There was a statistically significant difference between the available mouthwashes classified as cosmetic products compared to those registered as medicines and medical devices, Difference test ($p < 0.001$).

Table 1. List of available mouthwashes and their regulatory status

	Commercial name	**Regulatory status**
1	Alkmene Tea Tree Mouthwash	Cosmetic product
2	Alur Care Mouthwash Cool Mint	Cosmetic product
3	Alverde Pro Climate 5 in 1 Mundspülung	Cosmetic product
4	Aquafresh Big Teeth Mouthwash	Cosmetic product
5	Aquafresh Fresh & Minty	Cosmetic product
6	Astera Total All-in-One	Cosmetic product
7	Ben & Anna Natural Mouthwash Sensitive	Cosmetic product
8	Betadine Gargle	Medicine product
9	Bilka Dent Expert Classic Parodont Protect	Cosmetic product
10	Bilka Homeopathy Grapefruit Mouthwash	Cosmetic product
11	Colgate Cool Mint	Cosmetic product
12	Colgate Max White	Cosmetic product

13	Colgate Plax ICE	Cosmetic product
14	Colgate Plax Soft Mint	Cosmetic product
15	Colgate Plax White + Charcoal	Cosmetic product
16	Cosmos Organic People Mouthwash Coconut & Mint	Cosmetic product
17	Curaprox Perio Plus + Protect CHX 0.12	Cosmetic product
18	Curaprox Perio Plus Balance CHX 0.05	Cosmetic product
19	Curaprox Perio Plus Forte CHX 0.20	Cosmetic product
20	Curaprox Regenerate CHX 0.09	Cosmetic product
21	Doctor's Anti-Tartar Mouthwash	Cosmetic product
22	Doctor's Herbal Mouthwash	Cosmetic product
23	Doctor's Mint Mouthwash	Cosmetic product
24	Doctor's Propolis Mouthwash	Cosmetic product
25	Doctor's Smokers Mouthwash	Cosmetic product
26	Dontodent Junior Lerneffekt - spülung	Cosmetic product
27	Dontodent Junior Mund - spülung	Cosmetic product
28	Dontodent Neue Rezeptur Mundwasser Konzentrat	Cosmetic product
29	Dontodent Protect & Care 10 in 1 Rundumschutz	Cosmetic product
30	Dontodent Sensitive Intensiv - Schutz	Cosmetic product
31	Dontoent Zahnfleisch Intensiv - Pflege	Cosmetic product
32	Dr. Silver Mouthwash Total Care	Cosmetic product
33	Eco Denta Refresh & Protect Mouthwash	Cosmetic product
34	Edel+White Fresh+Protect	Cosmetic product
35	Elmex Caries Protection	Cosmetic product
36	Elmex Sensitive	Cosmetic product
37	ESI Aloe Fresh Collutorio	Cosmetic product
38	FrezyDerm Plaque & Tartar Mouthwash	Cosmetic product
39	FrezyDerm Sensitive Teeth Mouthwash	Cosmetic product
40	Gengigel Oral Solution	Medical device
41	Green Fresh Concentrate Mouthwash	Cosmetic product
42	Intermed Chlorhexil 0.12% Mouthwash	Cosmetic product
43	Intermed Chlorhexil Extra 0.20% Mouthwash	Cosmetic product
44	Intermed Kids Mouthwash	Cosmetic product
45	Intermed Unisept Mouthwash	Cosmetic product
46	Lacalut Aktiv	Cosmetic product
47	Lacalut Flora	Cosmetic product
48	Lacalut Micellar Sensitive Mouthwash	Cosmetic product

49	Lacalut Micellar Tartar Protection Micellar Water	Cosmetic product
50	Lacalut Micellar Whitening Mouthwash	Cosmetic product
51	Lacalut Multi-Effect Micellar Mouthwash	Cosmetic product
52	Lacalut Sensitive	Cosmetic product
53	Lacalut white	Cosmetic product
54	Limes Rosa Fresh Concentrate	Cosmetic product
55	Listerine Advanced Defence Sensitive	Medical device
56	Listerine Advanced White Mouthwash Mild Taste	Cosmetic product
57	Listerine Cool Mint	Cosmetic product
58	Listerine Fresh Burst	Cosmetic product
59	Listerine Green Tea Mild Taste	Cosmetic product
60	Listerine Natural Enamel protect	Cosmetic product
61	Listerine Naturals Sabor Suave	Cosmetic product
62	Listerine Smart Rinse	Cosmetic product
63	Listerine Teeth & Gum Defence	Cosmetic product
64	Listerine Total Care Clean Mint 6 in 1	Cosmetic product
65	Listerine Total Care Clean Mint 6 in 1 Mild Taste	Cosmetic product
66	Listerine Total Care Tartar Protect	Cosmetic product
67	Maxlab Silver Water	Cosmetic product
68	Natura Siberica Plaque Control & Fresh Breath	Cosmetic product
69	Natura Siberica Strong Teeth & Gums	Cosmetic product
70	Natura Siberica Whitening & Enamel Protection	Cosmetic product
71	Oral-B Gum & Enamel Care Fresh Mint	Cosmetic product
72	Oral-B Pro-Expert	Cosmetic product
73	Oralsept	Medicine product
74	Parodont Active	Cosmetic product
75	Parodontax Active Gum Health	Cosmetic product
76	Stomatidin	Medicine product

Table 2. Regulatory status of available mouthwashes

Regulatory status	**Number (percent)**
Cosmetic products	71 (93.43%)
Medicine products	3 (3.94%)
Medical devices	2 (2.63%)
Total	**76 (100%)**

Discussion

The term *oral hygiene product* is relatively new and describes mechanical devices and chemical compounds designed to provide the user with oral health and cosmetic benefits. The potential major health value of such oral hygiene products is the prevention of plaque-related diseases, such as caries, gingivitis, and periodontitis. The primary cosmetic benefits are breath refreshing and extrinsic stain control. Given the long-term history of oral hygiene products, control over the chemical compounds (products) and scientific evaluation of efficacy are very recent matters. Medicine laws in many countries demand extensive toxicological data on the ingredients used in oral hygiene products[23].

The cosmetics industry is one of the most dynamically developing sectors globally [24] and together with the pharmaceutical industry, they have a major contribution to human well-being[25].

As a result of many incidents throughout history, regulatory bodies have introduced new laws and guidelines that improve the quality, safety, and efficacy of medical products[26]. Their goal is to ensure that the products deliver their intended benefits without causing harm, which requires a meticulous and multifaceted approach to regulatory control[27].

The qualification of a substance-based product as a medicinal product, a medical device, or a cosmetic product can be challenging, with several products being considered borderline. Different regulatory authorities have their own specific set of regulations for the registration, approval, and control of the ingredients of these products[28–30].

Our study shows that most of the available mouthwashes on the market in the Republic of North Macedonia are classified as cosmetic products, which is consistent with national legislation where dental and oral care products are considered cosmetic products[31]. The National Law on Safety of Cosmetic Products defines a cosmetic product as any substance or product intended to be applied to various external parts of the human body (epidermis, hair, nails, lips, and external genital organs, or to the teeth and the mucous membranes of the oral cavity), for cleaning, perfuming, altering appearance, correcting body odors, and/or protecting or maintaining them in good condition[32].

A similar definition is given by Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products, where a cosmetic product is defined as any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair, nails, lips, and external genital organs) or with the teeth and the mucous membranes of the oral cavity, with the exclusive or primary aim of cleaning, perfuming, altering appearance, protecting, maintaining them in good condition, or correcting body odors[33]. The Regulation defines an oral product as a cosmetic product intended to be applied to the teeth or the mucous membranes of the oral cavity[33]. This act recognizes mouthwashes as oral products.

To ensure compliance through the single market regarding the categorization of products, the European Commission has published a series of guidelines and guides for the demarcation of products between cosmetic products and other product categories, to determine whether a product falls within the definition of Regulation 1223/2009 on cosmetic products. Namely, sometimes it is unclear whether a certain product, based on its characteristics and function, can be categorized as a cosmetic product according to the regulations governing cosmetic products or if it falls under other sectoral regulations. The European Commission published certain guidelines to facilitate the application of EU legislation, which include Guides on the scope of application of Regulation 1223/2009 on cosmetic products and Guides between the legislation of cosmetic products and biocides and medicines. While these guidelines are not legally binding, they serve to help categorize products. According to some documents, a mouthwash that presents antibacterial or antiseptic claims can be qualified as a cosmetic product, a biocidal product, or a medicinal product. A decision on the qualification of the products must be made by the national competent authorities on a case-by-case basis, taking into account all relevant elements, such as the presentation of the products, the ingredients, the mode of action, and the claims [34].

Sometimes, mouthwashes can be qualified as medical devices[35]. Our study shows that two of the commercially available mouthwashes (Gengigel Oral Solution, and Listerine Advanced Defense Sensitive) are classified as medical devices. The Regulation 2017/745 on medical devices (MDR) determines that devices composed of substances or combinations of substances intended to be introduced into the human body via a body orifice or applied to the skin, and

that are absorbed by or locally dispersed in the human body, are classified as class IIa if they are applied to the skin or if they are applied in the nasal or oral cavity as far as the pharynx, achieving their intended purpose in those cavities[36]. These mouthwashes found in the Macedonian market are also classified as medical devices in Serbia[37], Croatia[38], Bosnia and Herzegovina[39], and other regional countries.

Three out of the 76 mouthwashes were classified as medicinal products. These mouthwashes contain one of the following active substances: povidone-iodine, benzydamine, or hexetidine. According to the drug register maintained by the Agency for Medicines and Medical Devices (MALMED), these products are available without a prescription[40]. Povidone-iodine has antiseptic properties[41], while benzydamine possesses anti-inflammatory properties[42], and hexetidine also possesses antiseptic properties[43]. Marketing authorizations for medicines and medical devices intended for human use are fundamentally granted by a competent regulatory authority in the form of an official approval (license) for a specified time period. This authorization is based on a rigorous and comprehensive evaluation process that assesses scientific, clinical, quality, and cost-effectiveness factors[44].

In the USA, the Federal Food, Drug, and Cosmetic Act defines two main categories of products: cosmetics and drugs. The latter includes a sub-category of over-the-counter (OTC) drugs, which can be sold without a prescription[45]. The United States Food and Drug Administration has established guidelines indicating that mouthwashes with potential therapeutic properties should be registered as drugs rather than cosmetics[46]. The American Dental Association employs a dichotomous approach to mouthwash usage, classifying them as either cosmetic or therapeutic based on the presence or absence of a chemically active ingredient. Cosmetic mouthwashes are those that lack bactericidal or bacteriostatic properties and are primarily used for temporarily masking symptoms such as bad breath. These products are typically sold over the counter (OTC) and do not require a prescription for purchase, including some of the previously mentioned natural mouthwashes. Essential oil-containing antimicrobial mouthwashes are recognized as clinically effective against plaque and gingivitis and are also available OTC. Therapeutic mouthwashes, in contrast, contain active ingredients such as cetylpyridinium chloride, chlorhexidine, fluoride, or hydrogen peroxide, which provide antimicrobial effects. These mouthwashes must be dispensed by prescription, are intended for short-term use, and are designed to treat specific conditions. Research indicates that therapeutic mouthwashes can be effective in managing oral health issues[47,48].

Similarly, in Canada, products can be categorized as either cosmetics or over-the-counter (OTC) drugs, with natural health products (NHP) considered a subset of drugs. Japan features a unique categorization system, where beauty products are divided into two categories: cosmetics and quasi-drugs. In Australia, toothpaste and oral hygiene products are regulated as either therapeutic goods or cosmetics, depending on factors such as how the product is advertised, the claims made, its intended use, and its ingredients[49].

Nevertheless, regardless of their categorization, all cosmetic products, medicinal products, and medical devices placed on the market must be safe. In the Republic of North Macedonia, according to the Law on Medicines and Medical Devices, the Agency for Medicines and Medical Devices (MALMED) is mandated to establish and maintain a pharmacovigilance and materiovigilance system. The current law defines materiovigilance as a system designed to detect, collect, monitor, evaluate, and ensure the appropriateness of new safety data concerning medical devices and potential incidents of use. Pharmacovigilance is defined as a system applied to detect, collect, monitor, evaluate, and ensure the appropriateness of new safety data regarding medicines and their interactions. The Agency for Medicines and Medical Devices (MALMED) is responsible for establishing and maintaining the pharmacovigilance and materiovigilance systems. The pharmacovigilance and materiovigilance system for the holder of the marketing authorization for a medicine or medical device is organized by the responsible personnel of the marketing authorization holder[50]. Additionally, the rulebook on the method of reporting side effects during the use of medical devices outlines the types of reactions they can cause, the actions required from health professionals and suppliers, and the organization of the system for monitoring side effects and reactions from medical devices [51]. For cosmetic products, national regulations stipulate that only cosmetic products that fully meet safety requirements can be placed on the market. Cosmetic products that are imported must meet the safety requirements established

by law. The manufacturer placing the product on the market is responsible for the safety of the cosmetic product. The legal or physical entity conducting the marketing of the product is responsible for maintaining the product's safety in terms of storage methods and shelf life. Oversight of the application of the law is conducted by the Ministry of Health, while the State Sanitary and Health Inspectorate performs the inspection oversight regarding the implementation of the law[32].

EU law mandates that every marketing authorization holder, national competent authority, and the European Medicines Agency (EMA) establish and maintain a pharmacovigilance system. The overarching EU pharmacovigilance system functions through cooperation among EU Member States, the EMA, and the European Commission. In certain Member States, regional centers operate under the coordination of the national competent authority[52]. The Medical Device Regulation (MDR) was established as a new certification framework that imposes additional requirements, such as the obligation for manufacturers to designate a specific role within their organization responsible for regulatory compliance. It also introduces stricter measures, including enhanced post-market surveillance and vigilance, reflecting the evolving global medical device market. Specifically, these new requirements are designed to ensure user safety through improved transparency and better traceability of medical devices[53]. In addition, cosmetic products marketed in the European Union (EU) are held to high standards of safety and quality. Undesirable effects arising from the normal or reasonably foreseeable use of cosmetic products are rare, typically mild, and completely reversible. Companies have established procedures to respond effectively to reports of undesirable effects, which include recording, assessing, and understanding their nature to prevent future occurrences. This process is crucial for companies as it enhances post-marketing surveillance of cosmetic products and their performance in the marketplace. The primary objective of post-marketing surveillance is to protect consumer health by monitoring the incidence of undesirable effects (UE) and minimizing the risk of their reoccurrence. The evaluation of Serious Undesirable Effects (SUEs) includes the dissemination of information that can be utilized to prevent their recurrence or to mitigate the consequences of such effects. The EU Cosmetovigilance System aims to ensure a direct, prompt, and harmonized implementation of these actions across EU Member States, as opposed to addressing issues on a country-by-country basis. This system enhances the ability to manage and respond to undesirable effects effectively throughout the European Union[54].

Considering that the majority of mouthwashes available on the market in the Republic of North Macedonia are classified as cosmetic products, the question arises whether this classification is accurate and if their safety is guaranteed. In our view, the cosmetics industry has been striving for global regulatory harmonization over the past few decades. Mouthwashes are deemed safe and, thus, should be classified as cosmetic products. However, with the increasingly demanding and evolving global regulatory landscape, there is a pressing need for heightened vigilance among companies and manufacturers to ensure compliance. The significance of post-market surveillance, reporting adverse effects, addressing non-compliance, and implementing enforcement measures against responsible parties (such as withdrawing non-compliant products from the market or imposing financial penalties) cannot be overstated.

Conclusion

Most of the mouthwashes available on the market in the Republic of North Macedonia are classified as cosmetic products. Regardless of their classification, it is essential for mouthwashes to meet both national and international safety standards before being placed on the market. Additionally, ongoing vigilance is required following normal or reasonably foreseeable use of these products.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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