cosmetics

MDPI

Article

Microbiologically Contaminated and Over-Preserved Cosmetic Products According Rapex 2008–2014

Edlira Neza * and Marisanna Centini

Department of Biotechnologies, Chemistry and Pharmacy, University of Siena, Via Aldo Moro 2, Siena 53100, Italy; marisanna.centini@unisi.it

* Correspondence: edliraneza@yahoo.com; Tel.: +355-685-038-408

Academic Editors: Lidia Sautebin and Immacolata Caputo
Received: 25 December 2015; Accepted: 25 January 2016; Published: 30 January 2016

Abstract: We investigated the Rapid Alert System (RAPEX) database from January 2008 until week 26 of 2014 to give information to consumers about microbiologically contaminated cosmetics and over-preserved cosmetic products. Chemical risk was the leading cause of the recalls (87.47%). Sixty-two cosmetic products (11.76%) were recalled because they were contaminated with pathogenic or potentially pathogenic microorganisms. *Pseudomonas aeruginosa* was the most frequently found microorganism. Other microorganisms found were: Mesophilic aerobic microorganisms, *Staphylococcus aureus*, *Candida albicans*, *Enterococcus* spp., *Enterobacter cloacae*, *Enterococcus faecium*, *Enterobacter gergoviae*, *Rhizobium radiobacter*, *Burkholderia cepacia*, *Serratia marcescens*, *Achromabacter xylosoxidans*, *Klebsiella oxytoca*, *Bacillus firmus*, *Pantoea agglomerans*, *Pseudomonas putida*, *Klebsiella pneumoniae* and *Citrobacter freundii*. Nine cosmetic products were recalled because they contained methylisothiazolinone (0.025%–0.36%), benzalkonium chloride (1%), triclosan (0.4%) in concentrations higher than the limits allowed by European Regulation 1223/2009. Fifteen products were recalled for the presence of methyldibromo glutaronitrile, a preservative banned for use in cosmetics. Thirty-two hair treatment products were recalled because they contained high concentrations of formaldehyde (0.3%–25%).

Keywords: microbiologically contaminated; over-preserved cosmetics; formaldehyde; RAPEX

1. Introduction

The European Commission (EC) has an early warning system for safety management called the Rapid Alert System (RAPEX). In the database of this system we can find information about dangerous cosmetic products sold in EU markets. Dangerous cosmetic products pose a risk to the consumers due to the presence of certain substances which are banned or the use of which is restricted in these products under cosmetic legislation [1].

Cosmetic products are recognized to be substrates for the survival and development of a large variety of microorganisms, since they posses some of the nutrients that facilitate growth such as water, lipids, polysaccharides, alcohol, proteins, amino acids, glycosides, peptides and vitamins [2]. The presence of pathogenic microorganisms in cosmetic products can pose a health risk for consumers. The use of preservatives, Good Manufacturing Practices (GMP) and quality control programs has improved the quality, but several studies have reported cases of contaminated cosmetic products [3–8]. Studies have shown that the most frequently found microorganisms in cosmetics are *P. aeruginosa*, *K. oxytoca*, *B. cepacia*, *S. aureus*, *E. coli*, *C. albicans*, *E. gergoviae*, and *S. marcescens*, but also other bacteria, fungi, and yeasts. Skin and mucous membranes are protected from microorganisms; however, these may be damaged and slight trauma may be caused by the action of some cosmetics that may enhance microbial infection [9]. Research studies have shown cases of infections caused by contaminated

cosmetics [10–12]. According to SCCP's (Scientific Committee on Consumer Products) "Notes of Guidance", cosmetic products are divided into two different categories: (1) Products specifically intended for children under three years or to be used in the eye area and on mucous membranes and (2) other products. Products intended for use on babies and the eye area (category 1) should have not more than 10^2 Cfu/g or mL of aerobic mesophilic microorganism (other products not more than 10^3 Cfu/g or mL). *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans* or *Escherichia coli* must not be detectable in 0.5 g or 0.1 mL of product category 1 and in 0.1 g or 0.1 mL of product category 2 [13]. To prevent the microbial contamination of cosmetic products, chemical substances with known antimicrobial properties are used. The EU regulation 1223/2009 provides a list of allowed preservatives in cosmetic products with maximum concentrations in ready-for-use preparation. Preservatives are known as one of the most relevant allergens found in cosmetic products [14,15]. Studies suggest that the problem is much bigger because contact dermatitis prevalence appears to be underestimated [16]. In recent years a significant increase in cases of methylisothiazolinone contact allergy (MI) has been reported [17–21].

2. Experimental Section

We used the RAPEX database to find microbiologically contaminated cosmetic products from January 2008 until week 26 of 2014. We also selected recalled cosmetic products with high concentrations of preservatives.

3. Results and Discussion

3.1. Microbiologically Contaminated Cosmetics

The risks of recalled cosmetic products were divided in two categories: chemical and microbiological. Chemical risks were the leading cause of the recalls (87.47%). Sixty-two cosmetic products contaminated with microorganisms were recalled during this period. The most frequently found microorganism was the pathogenic *Pseudomonas aeruginosa* (35.48%). Other microorganisms found were: mesophilic aerobic microorganisms (bacteria, yeast and molds), *Burkholderia cepacia*, *Klebsiella oxytoca*, *Serratia marcescens*, *Enterobacter gergoviae*, *Enterobacter cloacae*, *Staphylococcus aureus*, *Achromabacter xylosoxidans*, *Rhizobium radiobacter*, *Candida albicans*, *Pantoea agglomerans*, *Citrobacter freundii*, *Pseudomonas putida*, *Enterococcus faecium* and *Klebsiella pneumoniae.* The types of cosmetic products contaminated were different: skin lightening products, eye creams, eye make-up products, children's shampoos, skin care products, baby creams, baby balms, toothpastes (Table 1). The recalled products were notified by 14 different countries and 41.67% of them were notified by Germany. The number of recalled contaminated cosmetic products was higher in the last two years (2013, 2014).

In 21 cosmetic products (33.87%), *Pseudomonas* were present, especially *Pseudomonas aeruginosa*. *P. aeruginosa* is a pathogenic Gram-negative bacteria frequently found in cosmetics but also in ophthalmic preparations and, as such, is responsible for a variety of infectious diseases affecting the eye and surrounding tissues (corneal ulcer, bacterial keratitis) [22–26]. Six hair shampoo products were contaminated with *P. aeruginosa* or *P. putida* and these products can come in contact with eyes. These bacteria are widely recognized as nosocomial infection–causing pathogens [27,28]. *P. aeruginosa* in some cases had showed resistance to preservatives in cosmetic products.

Burkholderia cepacia, an opportunistic pathogen, was found in five products: make-up remover, bath gel, mouth spray and mouth wash, body scrub products (4.1×10^5–100×10^5 Cfu/g). Other studies have showed that the presence of *B. cepacia* in products used for mouth hygiene has frequently been implicated in *B. cepacia* infection [29–31]. Contamination of cosmetics and pharmaceuticals with *B. cepacia* is also a frequent problem in the United States and it is a cause of major product recalls [32–34]. *B. cepacia* can cause diseases primarily among immuno-compromised populations [35].

Table 1. Microbiologically contaminated products.

Contaminated Product	Microorganisms	Cfu/g	Country of Origin
Shea butter	*P. aeruginosa*, *S. aureus*, *C. albicans*	1000	Germany
Children's make-up set	Mesophilic aerobic microorganism	1300	Hong Kong
Skin lightening product	*Aerobic mesophilic flora*	1083	Spain
Make-up remover	*Burkholderia cepacia*	Not specified	Austria
Massage cream	*S. aureus*	Not specified	Austria
Cleasing milk	Total aerobic mesophile (yeast and mold)	430,000/820,000/6,000,000/7,500,000	Italy
Cotton buds	*P. aeruginosa*	Not specified	Turkey
Natural hair dye	Mesophilic aerobic microorganism	140,000/19,000/26,000	Czech Republic
Skin lotion	*P. aeruginosa*	19,000,000	Hungary
Massage gel	Enterobacteriaceae	5,100,000	Thailand
Eye cream	*E. gergoviae*	290,000	Israel
Herbal tooth powder	*P. aeruginosa*, *K. pneumonie*, *E. faecium*	540,000	India
Mouthwash	Aerobic mesophile	Not specified	United Kingdom
Toothpaste	Mesophilic aerobic microorganisms	1,100,000	Not specified
Shampoo/shower gel	*E. cloaceae-C. freundii*, *P. putida*, *K. pneumoniae*	1,100,000/19,000,000	Germany
Body paint powder	*P. aeruginosa*	3000/15,000	United Kingdom
Henna Hand paint	*P. agglomerans*, *B. firmus*	2,600,000	India
Hand soap	*K. oxytoca*	High	Unknown
Toothpaste	Enterobacteriaceae	10,000/1600	Ireland
Bath gel	*B. cepacia*	10,000,000	China
Mouth spray and mouth wash	*B. cepacia*	Not specified	Germany
Hand cream	*P. aeruginosa*	Not specified	Switzerland
Eye make-up	Aerobic mesophilic flora	5000	Pakistan
Skin care product	Aerobic mesophilic flora, *A. xylosoxidans*	3,000,000	Poland

Table 1. *Cont.*

Contaminated Product	Microorganisms	Cfu/g	Country of Origin
Body scrub	Mesophilic bacteria, *B. cepacia*	480,000	China
Hand washing paste	*P. aeruginosa*	8,200,000	Germany
Make-up set	Mould	Not specified	China
Rose facial milk	*P. aeruginosa*	600	Germany
Shampoo-Hair	*P. aeruginosa*	570,000	Philippines
Sun cream	*P. aeruginosa*	Not specified	Czech Republic
Bath milk for babies	*S. marcescens*	Not specified	Germany
Tattoo ink	Aerobic mesophiles, *P. aeruginosa*, yeasts	3,600,000/1,100,000/900,000	United States
Anti-wrinkle serum	*Pseudomonas.spp*	15,000	United States
Natural hair dye	Not specified	300,000	Russian Federation
Fitness gel	*B. cepacia*	410,000–520,000	Turkey
Eye contour cream	*R. radiobacter*	Not specified	France
Lubrificant	Mesophilic microorganisms (yeast)	Not specified	France
Herbal shampoo	*P. aeruginosa*	Not specified	India
Hair dye	Mesophilic aerobic microorganism	Not specified	Czech Republic
Skin cream	*P. aeruginosa*, *mesophilic bacteria*	13,000	Germany
Hair dye	Mesophilic aerobic microorganism	Not specified	Czech Republic
Hair dye	Mesophilic aerobic microorganism	Not specified	Czech Republic
Baby cream	Not specified	3168	Germany
Hair dye	Mesophilic aerobic microorganism	Not specified	India
Hair dye	Mesophilic aerobic microorganisms	Not specified	India
Shower gel	Aerobic mesophilic bacteria	50,000	United Kingdom
Hair dye	Mesophilic aerobic microorganisms	370,000	Germany

Table 1. *Cont.*

Contaminated Product	Microorganisms	Cfu/g	Country of Origin
Marmot fat	Aerobic mesophilic bacteria, *P. aeruginosa*	760,000/610,000	Denmark
Children's shampoo	*E. gergoviae*	Not specified	Unknown
Shampoo and bath gel	Mesophilic aerobic microorganisms	Not specified	Unknown
Skin cream	Aerobic mesophilic bacteria, *E. gergoviae*	120,000	Germany
Liquid hand soap	Mesophilic aerobic microorganisms	Not specified	Unknown
Hair dye	Mesophilic aerobic microorganisms	90,000	Germany
Hand cleaning paste	Aerobic mesophlic bacteria , *E. gergoviae*	19,000,000	Unknown
Baby balm	*P. aeruginosa*	Not specified	Belgium
Tinted day cream	*P. aeruginosa*	3,000,000	Italy
Skin cream	*P. aeruginosa*, aerobic mesophilic bacteria	60,000/2,600,000	Germany
Shampoo	*P. aeruginosa*, aerobic mesophilic bacteria	27,000	Germany
Hair shampoo	*P. putida*, *P. aeruginosa*	24,000/8700	Austria
Cream	*E. gergoviae*	4,400,000/160,000	Germany
Sun lotion	*E. cloacae*, *E. faecium*, *E.* spp.	8,000,000	Austria
Hair shampoo	*P. aeruginosa*	10,000	Germany

Staphylococcus aureus was found in two products: shea butter and massage cream. *S. aureus* is also one of the most frequently found contaminants in cosmetic products [36]. *S. aureus* is a Gram-positive microorganism and a potential human pathogen which can cause impetigo and conjunctivitis [37]. *Enterobacter gergoviae* was present in eye creams and children's cosmetic products (shampoo, foam soap, gel, creams and lotions, skin cream, *etc.*) at concentrations of 1.6×10^5–44×10^5 Cfu/g. *E. gergoviae* is naturally resistant to parabens at the concentrations used in cosmetics [38,39]. The germs are often resistant to antibiotics and this makes treatment more difficult. *Serratia marcescens* is a Gram-negative bacillus (Enterobacteriaceae). *S. marcescens* was generally considered non-pathogenic for humans [40], but since the 1950s has become an important cause of nosocomial infection [41]. Infants are at the greatest risk of *S. marcescens* infection (severe septicemia) or colonization [42–45]. Baby death has been reported from *S. marcescens* meningitis and septicemia after use of contaminated baby shampoo [46]. One recalled product was bath milk for babies and it was contaminated with *S. marcescens*. Two recalled products were contaminated with *Klebsiella pneumoniae*, a shampoo/shower gel and an herbal tooth powder. *Klebsiella pneumonia*, a Gram-negative bacterium in the Enterobacteriaceae family, is a human pathogen and can cause severe fulminating pneumonia [47]. *Klebsiella* present in hand creams and liquid soaps in the past has caused epidemic septicemia in patients with intravenous catheters [48]. Molds and yeasts were also present in two products. A make-up set was contaminated with mold which, according to RAPEX, may cause irritation, inflammation to skin around the eye, respiratory infection if inhaled or loss of eye sight. *Candida albicans* was isolated in one product (shea butter, Germany).

Rhizobium radiobacter (known as *Agrobacterium radiobacter*) was present in an eye contour cream product. It is usually of low virulence in humans and rarely acts as an opportunistic human pathogen [49].

3.2. Over-Preserved Cosmetic Products

Twenty-four cosmetic products were recalled because they contained methylisothiazolinone (0.025%–0.36%), methyldibromo glutaronitrile, triclosan (0.4%) and benzalkonium chloride (1%) in concentrations higher than the limits allowed by European Regulation 1223/2009 (Table 2).

Table 2. Over-preserved cosmetics.

Product	Preservative	Country of Origin	Concentration
Shower Gel	Methyldibromo glutaronitrile	Russia	Not specified
Skin cream	Methyldibromo glutaronitrile	Spain	Not specified
Shampoo	Methyldibromo glutaronitrile	Italy	Not specified
Shampoo "Tea tree oil"	Methyldibromo glutaronitrile	Russia	Not specified
Shower gel	Methyldibromo glutaronitrile	Russia	Not specified
Hair straightening treatment	Methyldibromo glutaronitrile	United States	Not specified
Skin lightening cream	Methyldibromo glutaronitrile	South Africa	Not specified
Shampoos and haircare products	Methyldibromo glutaronitrile	Italy	Not specified
Shower gel	Methyldibromo glutaronitrile	Turkey	Not specified
Wetwipes	Methyldibromo glutaronitrile	Turkey	Not specified
Children's shampoo	Methyldibromo glutaronitrile	Ukraine	Not specified
Children's shampoo	Methyldibromo glutaronitrile	Ukraine	Not specified
Liquid cleanser	Methyldibromo glutaronitrile	Italy	Not specified
Creams	Methyldibromo glutaronitrile	Germany	Not specified
Hair straightening treatment	Methyldibromo glutaronitrile	United States	Not specified
Facial mask	Methylisothiazolinone	Russian Federation	0.03%
Baby care cream	Methylisothiazolinone	Russian Federation	0.027%
Body mousse	Methylisothiazolinone	Russian Federation	0.028%
Body butter	Methylisothiazolinone	Russian Federation	0.026%
Foot cream	Methylisothiazolinone	Russia	0.03%–0.08%
Foot cream	Methylisothiazolinone	Russian Federation	0.36%
Facial mask	Methylisothiazolinone	Russian Federation	0.025%
Eyelash enhanser	Benzalkonium chloride	China	1%
Children cream	Triclosan	Spain	0.4%

Fifteen cosmetic products recalled (shower gels, skin creams, shampoo and children's shampoo, wet wipes) contained methyldibromo glutaronitrile. This preservative has been banned in EU countries because of increasing rates of contact allergy [50–53].

Seven cosmetic products recalled contained the preservative methylisothiazolinone (0.01% or 0.0015% of a mixture in the ratio 3:1 of methylchloroisothiazolinone and methylisothiazolinone) in excess (0.025%–0.36%) of the approved concentration limit. The country of origin of the products was the Russian Federation. MI is a sensitizing agent and may cause skin sensitization and allergic skin reactions when it exceeds the approved maximum concentration [54,55]. MI is also is an emerging allergen in the pediatric population. Wet wipes with MI were frequently the cause of allergy contact dermatitis [56–60].

One product contained benzalkonium chloride in a concentration 10 times higher than the maximum allowed (eyelash enhancer, 1%). Benzalkonium chloride is a well-recognized irritant for skin and eyes at concentrations greater than 0.1%. According to EU regulation 1223/2009, contact of benzalkonium chloride with eyes should be avoided.

Thirty-two cosmetic products contained formaldehyde (0.3%–25%) in concentrations higher than the limits allow (Table 3). All products recalled were hair treatment products. In the European Union, formaldehyde is not authorized as an active ingredient in hair straightening products. Formaldehyde is a chemical substance used in cosmetics as a preservative for its antimicrobial properties. According to Cosmetics Regulation 1223–2009 Annex V, formaldehyde can be used in oral products in concentrations of not more than 0.1% (free formaldehyde) and 0.2% in other products. Formaldehyde can also be used in nail-hardening products at concentrations of up to 5% (Annex III).

Table 3. Cosmetic products with high concentration of formaldehyde.

Product	Concentration	Country of Origin
Stabilizer for cosmetics	25%	Spain
Hair straightening treatment	1.6%	Italy
Hair treatment product	3.5%	United States
Hair treatment product	0.3%	United States
Hair treatment product	2.89%	Brazil
Hair straightening	6.7%	Brazil
Hair treatment product	7.0%	Brazil
Hair treatment	1.6%	United States
Hair treatment	1.7%	United States
Hair straightening product	2.15%	China
Hair treatment	1.7%	Brazil
Hair treatment	1.8%, 1.9%	United States
Hair treatment product	1.77%	Italy
Hair treatment	1.7%, 2%	United States
Hair treatment product	0.5%, 0.8%	Brazil
Hair treatment product	0.9%, 1.5%, 1.6%, 1.7%	Brazil
Hair straightening treatment	Free formaldehyde 8.85% and 9.5%	United States
Hair treatment product	2.64%	Brazil
Hair treatment product	0.61%	Brazil
Hair treatment	Free formaldehyde 1.9% and 1.7%	United States
Hair treatment	2.0%	United Kingdom
Hair treatment product	7.7% free and liberated formaldehyde and 7.4% free formaldehyde	Brazil
Hair treatment product	2.3%	Unknown
Hair treatment products	1.0%, 1.3%, 1.7%, 10.8%	Mexico
Hair treatment product	0.95%, 0.7%, 2.3%, 2.4%, 2.5%, 2.6%	Brazil
Hair straightening product	0.98%	Brazil
Cosmetics pack	0.7%	Brazil
Hair straightener	2.6%	United States
Hair straightening treatment	0.49%	United States
Hair lotion	2%	Italy
Hair treatment products	>1.2%	United States
Hair treatment product	1.4%	Brazil

Formaldehyde is classified as a carcinogen [61,62]. Some epidemiologic studies have also found increased numbers of nasopharyngeal carcinoma and leukemia in humans exposed to formaldehyde [63].

4. Conclusions

European consumers are exposed to microbiologically contaminated and over-preserved cosmetic products. Hair treatment products with high concentrations of formaldehyde were also found. These products may pose a health risk to consumers. Measures must be taken to guarantee the safety of cosmetic products.

Author Contributions: The authors have equally contributed in data analyzing and paper writing.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Song, J.B.; Ahn, I.Y.; Cho, K.T.; Kim, Y.J.; Kim, H.S.; Lee, B.M. Development and application of risk management system for consumer products in compliance with global harmonization. *J. Toxicol. Environ. Health B. Crit. Rev.* **2013**, *16*, 1–16. [CrossRef] [PubMed]
2. Herrera, G.A. Microbiological analysis of cosmetics. *Methods Mol. Biol.* **2004**, *268*, 293–295. [PubMed]
3. Lundov, M.D.; Zachariae, C. Recalls of microbiologically contaminated cosmetic in EU from 2005 to May 2008. *Int. J. Cosmet. Sci.* **2008**, *6*, 471–474. [CrossRef] [PubMed]
4. Wong, S.; Street, D.; Delgado, S.I.; Klontz, K.C. Recalls of foods and cosmetics due to microbial contamination reported to the U.S. Food and Drug Administration. *J. Food Prot.* **2000**, *63*, 1113–1116. [PubMed]
5. Behravan, J.; Bazzar, F.; Malaekeh, P. Survey of bacteriological contamination of cosmetic creams in Iran (2000). *Int. J. Dermatol.* **2005**, *44*, 482–485. [CrossRef] [PubMed]
6. Hugbo, P.B.; Onyekweli, A.O.; Igwe, I. Microbial contamination and preservative capacity of some brands of cosmetic creams. *Trop. J. Pharm. Res.* **2003**, *2*, 229–234. [CrossRef]
7. Shaqra, Q.; Al-Groom, R. Microbiologically quality of hair and skin care cosmetics manufactured in Jordan. *Int. Biodeterior. Biodegrad.* **2012**, *69*, 69–72.
8. Mwambete, K.D.; Simon, A. Microbiological quality and preservative capacity of commonly available cosmetics in Dar es Salaam, Tanzania. *J. Pharm. Sci.* **2010**, *13*, 3–11.
9. Scientific Committee on Consumer Products. The SCCP's Notes of Guidance for the Testing of Cosmetic Ingredients and Their Safety Evaluation. Available online: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_006.pdf (accessed on 11 November 2015).
10. Ashour, E.; Abdelaziz, A.A.; Hefni, H.; El-Tayeb, M. Microbial contamination of cosmetics and personal care items in Egypt—Body lotion and talcum powders. *J. Clin. Pharm. Ther.* **1989**, *14*, 207–212. [CrossRef]
11. Mpuchane, S.F.; Ekosse, G.E.; Gashe, B.A. Miscrobiological contamination of southern African medicinal and cosmetic clays. **2010**, *20*, 27–41. [PubMed]
12. Baird, R.M. Bacteriological contamination of products used for the skin care in babies. *Int. J. Cosmet. Sci.* **1984**, *6*, 85–90. [CrossRef] [PubMed]
13. Guidelines on Microbial Quality Management. 1997. Available online: https://www.cosmeticseurope.eu/publications-cosmetics-europe-association/guidelines.html?view=item&id=28 (accessed on 13 September 2015).
14. Timm-Knudson, V.L.; Johnson, J.S.; Ortiz, K.J.; Yiannias, J.A. Allergic contact dermatitis to preservatives. *Dermatol. Nurs.* **2006**, *18*, 130–136. [PubMed]
15. Maier, L.E.; Lampel, H.P.; Bhutani, T.; Jacob, S.E. Hand dermatitis: A focus on allergic contact dermatitis to biocides. *Dermatol. Clin.* **2009**, *27*, 251–264. [CrossRef] [PubMed]
16. Hamilton, T.; de Gannes, G.C. Allergic contact dermatitis to preservatives and fragrances in cosmetics. *Skin Ther. Lett.* **2011**, *16*, 1–4.
17. Maio, P.; Carvalho, R.; Amaro, C.; Santos, R.; Cardoso, J. Contact allergy to methylchoroisothiazolinone/methylisothiazolinone (MCI/MI): Findings from a contact dermatitis unit. *Cutan. Ocul. Toxicol.* **2012**, *31*, 151–153. [CrossRef] [PubMed]

18. Castanedo-Tardana, M.P.; Zug, K.A. Methylisothiazolinone. *Dermatitis* **2013**, *24*, 2–6. [CrossRef] [PubMed]
19. García-Gavín, J.; Vansina, S.; Kerre, S.; Naert, A.; Goossens, A. Methylisothiazolinone, an emerging allergen in cosmetics? *Contact Dermat.* **2010**, *63*, 96–101. [CrossRef] [PubMed]
20. Macias, V.C.; Fernandes, S.; Amaro, C.; Santos, R.; Cardoso, J. Sensitization to methylisothiazolinone in a group of methylchloroisothiazolinone/methylisothiazolinone allergic patients. *J. Cutan. Ocul. Toxicol.* **2013**, *32*, 99–101. [CrossRef] [PubMed]
21. Palmer, M.J.; Nixon, R. Polysensitisation in a laboratory scientist associated with allergic contact dermatitis from methylisothiazolinone in skin cleansers. *Australas. J. Dermatol.* **2014**, *23*, 98–102. [CrossRef] [PubMed]
22. Tenenbaum, S. Pseudomonas in cosmetics. *J. Soc. Cosmet. Chem.* **1967**, *18*, 797–807.
23. Reid, F.R.; Wood, T.O. Pseudomonas corneal ulcer. The causative role of contaminated eye cosmetics. *Arch. Ophthalmol.* **1979**, *97*, 1640–1641. [CrossRef] [PubMed]
24. Kreger, A.S. Pathogenesis of *Pseudomonas aeruginosa* ocular diseases. *Rev. Infect. Dis.* **1983**, *5*, 931–935. [CrossRef]
25. Hazlett, L.D. Corneal response to *Pseudomonas aeruginosa* infection. *Prog. Retin. Eye Res.* **2004**, *23*, 1–30. [CrossRef] [PubMed]
26. Blumenfeld, O.; Nathansohn, N.; Yeshurun, I.; Ashkenazi, I. Eye cosmetics-the beauty and the beast. *Harefuah* **2005**, *144*, 357–362. [PubMed]
27. Amemiya, K.; Taguchi, F. Bacterial contamination of hair washing liquids. *J. Jpn. Assoc. Infect. Dis.* **1994**, *68*, 177–182. [CrossRef]
28. Morrison, A.J.; Wenzel, R.W. Epidemiology of Infections due to *Pseudomonas aeruginosa*. *Clin. Infect. Dis.* **1984**, *6*, 627–642. [CrossRef]
29. Matrician, L.; Ange, G.; Burns, S.; Fanning, W.L.; Kioski, C.; Cage, G.D.; Komatsu, K.K. Outbreak of nosocomial *Burkholderia cepacia* infection and colonization associated with intrinsically contaminated mouthwash. *Infect. Control Hosp. Epidemiol.* **2000**, *21*, 739–741. [CrossRef] [PubMed]
30. Martin, M.; Winterfeld, I.; Kramme, E.; Ewert, I.; Sedemund-Adib, B.; Mattner, F. Outbreak of *Burkholderia cepacia* complex caused by contaminated alcohol-free mouthwash. *Anaesthesist* **2012**, *61*, 25–29. [CrossRef] [PubMed]
31. Molina-Cabrillana, J.; Bolaños-Rivero, M.; Alvarez-León, E.E.; Martín Sánchez, A.M.; Sánchez-Palacios, M.; Alvarez, D.; Sáez-Nieto, J.A. Intrinsically contaminated alcohol-free mouthwash implicated in a nosocomial outbreak of *Burkholderia cepacia* colonization and infection. *Am. J. Infect. Control* **1996**, *24*, 389–395. [CrossRef] [PubMed]
32. Jimenez, L.; Smalls, S. Molecular Detection of *Burkholderia cepacia* in Toiletry, Cosmetic, and Pharmaceutical Raw Materials and Finished Products. *J. AOAC Int.* **2000**, *83*, 963–966. [PubMed]
33. Jimenez, L. Microbial diversity in pharmaceutical product recalls and environments. *PDA. J. Pharm. Sci. Technol.* **2007**, *61*, 383–399. [PubMed]
34. Irwin, A.E.; Price, C.S. More than skin deep: Moisturizing body milk and *Burkholderia cepacia*. *Crit. Care* **2008**, *12*, 115. [CrossRef] [PubMed]
35. Torbeck, L.; Raccasi, D.; Guilfoyle, D.E. *Burkholderia cepacia*: This Decision Is Overdue. PDA. *J. Pharm. Sci. Technol.* **2011**, *65*, 535–543. [CrossRef] [PubMed]
36. Lundov, M.D.; Johansen, D.J.; Zachariae, C.; Moesby, L. Creams Used by Hand Eczema Patients are often Contaminated with *Staphylococcus aureus*. *Acta Derm. Venereol.* **2009**, *92*, 441–442. [CrossRef] [PubMed]
37. Brannan, K.D. *Cosmetic Microbiology: A Practical Handbook*; CRC Press Taylor & Francis Group: New York, NY, USA, 1997.
38. Périamé, M.; Pagès, J.M.; Davin-Regli, A. *Enterobacter gergoviae* adaptation to preservatives commonly used in cosmetic industry. *Int. J. Cosmet. Sci.* **2014**, *36*, 386–395. [CrossRef] [PubMed]
39. Davin-Regli, A.; Chollet, R.; Bredin, J.; Chevalier, J.; Lepine, F.; Pagès, J.M. *Enterobacter gergoviae* and the prevalence of efflux in parabens resistance. *J. Antimicrob. Chemother.* **2006**, *57*, 757–760. [CrossRef] [PubMed]
40. Scharf, J.W.; Wild, F.; Guggenbichler, J.P. Infection with *Serratia marcescens* in newborn infants. Clinical aspects, therapy and disease course. *Monatsschrift Kinderheilkd.* **1991**, *139*, 695–698.
41. Hejazi, A.; Falkiner, F.R. *Serratia marcescens*. *J. Med. Microbiol.* **1997**, *46*, 903–912. [CrossRef] [PubMed]

42. Van Ogtrop, M.L.; van Zoeren-Grobben, D.; Verbakel-Salomons, E.M.; van Boven, C.P. *Serratia marcescens* infections in neonatal departments: Description of an outbreak and review of the literature. *J. Hosp. Infect.* **1997**, *36*, 95–103. [CrossRef]
43. Voelz, A.; Müller, A.; Gillen, J.; Le, C.; Dresbach, T.; Engelhart, S.; Exner, M.; Bates, C.J.; Simon, A. Outbreaks of *Serratia marcescens* in neonatal and pediatric intensive care units: Clinical aspects, risk factors and management. *Int. J. Hyg. Environ. Health* **2010**, *213*, 79–87. [CrossRef] [PubMed]
44. Archibald, L.K.; Corl, A.; Shah, B.; Schulte, M.; Arduino, M.J.; Aguero, S.; Fisher, D.J.; Stechenberg, B.W.; Banerjee, S.N.; Jarvis, W.R. *Serratia marcescens* outbreak associated with extrinsic contamination of 1% chlorxylenol soap. *Infect. Control Hosp. Epidemiol.* **1997**, *18*, 704–709. [CrossRef] [PubMed]
45. Hirooka, T.M.; Fontes, R.B.; Diniz, E.M.; Pinto, F.C.; Matushita, H. Cerebral abscess caused by *Serratia marcescens* in a premature neonate. *Arq. Neuropsiquatri.* **2007**, *65*, 1018–1021. [CrossRef]
46. Madani, T.A.; Alsaedi, S.; James, L.; Eldeek, B.S.; Jiman-Fatani, A.A.; Alawi, M.M.; Marwan, D.; Cudal, M.; Macapagal, M.; Bahlas, R.; *et al*. *Serratia marcescens*-contaminated baby shampoo causing an outbreak among newborns at King Abdulaziz University Hospital, Jeddah, Saudi Arabia. *J. Hosp. Infect.* **2011**, *78*, 16–19. [CrossRef] [PubMed]
47. Parker, M.T. The clinical significance of the presence of micro-organisms pharmaceutical and cosmetic preparations. *J. Soc. Cosmet. Chem.* **1972**, *3*, 415–426.
48. Anelich, L.E.; Korsten, L. Survey of micro-organisms associated with spoilage of cosmetic creams manufactured in South Africa. *Int. J. Cosmet. Sci.* **1996**, *18*, 25–40. [CrossRef] [PubMed]
49. Lai, C.C.; Teng, L.J.; Hsueh, P.R.; Yuan, A.; Tsai, K.C.; Tang, J.L. Clinical and microbiological characteristics of Rhizobium radiobacter infections. *Clin. Infect. Dis.* **2004**, *38*, 149–153. [CrossRef] [PubMed]
50. Basketter, D.A. Methyldibromo glutaronitrile: Skin sensitization and quantitative risk assessment. *Cutan. Ocul. Toxicol.* **2010**, *29*, 4–9. [CrossRef] [PubMed]
51. Aakhus, A.E.; Warshaw, E.M. Allergy to methyldibromo glutaronitrile/phenoxyethanol (Euxyl K 400): Regulatory issues, epidemiology, clinical characteristics, and management. *Dermatitis* **2011**, *22*, 127–140. [PubMed]
52. Van Ginkel, C.J.; Rundervoort, G.J. Increasing incidence of contact allergy to the new preservative 1,2-dibromo-2,4-dicyanobutane (methyldibromo glutaronitrile). *J. Dermatol.* **1995**, *132*, 918–920. [CrossRef]
53. Jensen, C.D.; Johansen, J.D.; Menné, T.; Andersen, K.E. Methyldibromoglutaronitrile in rinse-off products causes allergic contact dermatitis: An experimental study. *Br. J. Dermatol.* **2004**, *150*, 90–95. [CrossRef] [PubMed]
54. Hosteing, S.; Meyer, N.; Waton, J.; Barbaud, A.; Bourrain, J.L.; Raison-Peyron, N.; Felix, B.; Milpied-Homsi, B.; Ferrier Le Bouedec, M.C.; Castelain, M.; *et al*. Outbreak of contact sensitization to methylisothiazolinone: An analysis of French data from the REVIDAL-GERDA network. *Cont. Derm.* **2014**, *70*, 262–269. [CrossRef] [PubMed]
55. Isaksson, M.; Hauksson, I.; Hindsén, M.; Pontén, A.; Svedman, C.; Bruze, M. Methylisothiazolinone Contact Allergy is Rising to Alarming Heights Also in Southern Sweden. *Acta Derm. Venereol.* **2015**, *95*, 31–34. [CrossRef] [PubMed]
56. Admani, S.; Matiz, C.; Jacob, S.E. Methylisothiazolinone: A case of perianal dermatitis caused by wet wipes and review of an emerging pediatric allergen. *Pediatr. Dermatol.* **2014**, *31*, 350–352. [CrossRef] [PubMed]
57. Madsen, J.T.; Andersen, K.E. Airborne allergic contact dermatitis caused by methylisothiazolinone in a child sensitized from wet wipes. *Cont. Derm.* **2014**, *70*, 183–184. [CrossRef] [PubMed]
58. Chang, M.W.; Nakrani, R. Six children with allergic contact dermatitis to methylisothiazolinone in wet wipes (baby wipes). *Pediatrics* **2014**, *133*, 434–438. [CrossRef] [PubMed]
59. Foote, C.A.; Brady, S.P.; Brady, K.L.; Clark, N.S.; Mercurio, M.G. Vulvar dermatitis from allergy to moist flushable wipes. *J. Low Genit. Tract. Dis.* **2014**, *18*, 16–18. [CrossRef] [PubMed]
60. Boyapati, A.; Tam, M.; Tate, B.; Lee, A.; Palmer, A.; Nixon, R. Allergic contact dermatitis to methylisothiazolinone: Exposure from baby wipes causing hand dermatitis. *Australas. J. Dermatol.* **2013**, *54*, 264–267. [CrossRef] [PubMed]

61. Griffin, V. Formaldehyde: Hazard alert on a possible human carcinogen. *Qld. Nurse* **1990**, *9*, 14–15. [PubMed]
62. Blackwell, M.; Kang, H.; Thomas, A.; Infante, P. Formaldehyde: Evidence of carcinogenicity. *Am. Ind. Hyg. Assoc. J.* **1981**, *42*, 34–46.
63. Swenberg, J.A.; Moeller, B.C.; Lu, K.; Rager, J.E.; Fry, R.C.; Starr, T.B. Formaldehyde carcinogenicity research: 30 years and counting for mode of action, epidemiology, and cancer risk assessment. *Toxicol. Pathol.* **2013**, *41*, 181–189. [CrossRef] [PubMed]