

"Promoting the autonomous implementation of the European framework agreement on occupational health and safety in the hairdressing sector" VS/2019/0440

Submitted by

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1 Preamble

The present paper consists of two parts, the first one describing the evidence which was retrieved in this project (Medical Reference Document) and the second one describing how to put the generated evidence into practical use and also addressing future research methods and targets (Methodological Note).

2 Introduction

Hairdressers are in contact with many hazardous and toxic agents, which entail different occupational health risks such as skin damage, respiratory problems, reproductive disorders, various forms of cancer, etc. Exposure can occur at the level of the skin as well as at the level of the respiratory tract. One major challenge in the health risk assessment in the hairdressing sector is that the occupational exposure is subject to change due to changing compositions of products at work. Research has shown that up to 70% of hairdressers suffer from work-related skin damage, mostly dermatitis, at some point during their career. The most important risk factors for developing occupational skin diseases (OSD) are wet work and occupational contact to irritants and allergens. In Europe, OSD represent up to 40% of all reported occupational diseases, and the often chronic course causes extensive suffering for the affected workers (Alfonso et al., 2017). The economic burden of OSD in the EU exceeds \in 5 billion p.a., spent on treatment, compensation, and loss of productivity (Ring, J, 2017). The chronic course of OSD may result in job loss and long-term unemployment (Armstrong et al., 2022).

Other occupational health problems of hairdressers are respiratory disorders related to inhalation exposure to hazardous chemicals from the used products. Aerosols are common in the hairdressing industry and can enter the lungs depending on the particle size. Hairdressers and hairdressing apprentices are thus prone to irritation of the upper airways. There is also some evidence that hairdressers develop chronic inflammation of the lower airways due to the exposure to chemicals with irritative and/or sensitizing properties. Furthermore, epidemiological studies have investigated carcinogenic and reproductive effects in hairdressing trade.

The European Cosmetics Regulation, adopted in 2009, is primarily focused on protecting consumers, with just a few provisions for professional users. The Scientific Committee on Consumer Safety (SCCS) does not consider risk assessment of occupational exposures as it does not have a mandate to do so. The SCCS therefore only deals with consumer aspects where

the consumer represents the general public in the usual sense. While consumers use hair cosmetic products mostly for just a few minutes a day, hairdressers may be exposed to them eight hours a day, five or six days a week, throughout their working lives. Hence, the SCCS opinions usually do not address the marked differences in exposure to chemical substances between a professional hairdresser and a consumer. Normally SCCS only considers the risk for consumers, however, they may state in their opinions that occupational exposure should be addressed.

In view of the above, there was a clear need for a systematic, up-to-date summary of available literature evidence in order to provide the scientific basis for protection of hairdressers' health. For example, relevant information on the incidence of respiratory disorders caused by occupational exposure to hair bleaches and other hairdressing chemicals with respiratory adverse effects are still missing.

This paper is the result of extensive literature research undertaken from December 2020 to May 2022 by a consortium of five project partners from Germany, Denmark, Croatia, and the Netherlands. The undertaken research was commissioned by the European Social Partners in Hairdressing, namely UNI Europa Hair & Beauty and Coiffure EU in the framework of the project VS/2019/0440 "Promoting the autonomous implementation of the European framework agreement on occupational health and safety in the hairdressing sector". It presents relevant findings related to the health risk from exposure of hairdressers pertaining to hair cosmetic products. By means of eight systematic literature and scoping reviews research, evidence from 2000-2021 was analyzed and evaluated. The reviews focused on substances (see Table 1) identified as most hazardous cosmetic ingredients having (potential) harmful outcomes on hairdressers' skin, systemic toxicity, respiratory, carcinogenic and reproductive effects. Based on the findings, a number of recommendations with regard to preventive and regulatory measures are made for future considerations (see Methodological Note, item 2). The paper also discusses innovative research methods for the evaluation of the impact of cosmetic substances on hairdressers.

3 Medical Reference Document (MRD)

In this Medical Reference Document you will find essential, scientifically-based background information.

3.1 Selected substances and approach

Following initial expert judgements within the project consortium about potentially hazardous types of products, a DELPHI survey was subsequently conducted shortlisting 33 substances. Feedback was provided by 48 of 121 invited experts (epidemiologists, dermatologists, toxicologists, etc.) (response: 40 %) resulting in a list of substances to be taken into consideration as shown in Table 1.

Table 1: List of most relevant product groups in hairdressing with substances covered by the different types of scientific reviews

	Product category	Substance(s)
1	Oxidative hair dyes/colorants	 <i>p</i>-phenylenediamine (PPD; CAS no. 106-50-3) and its salts (CAS no. 624-18-0, 16245-77-5)
		 toluene-2,5-diamine (PTD; CAS no. 95-70-5) and its sulfate (CAS no. 615-50-9)
		 2-methoxymethyl-PPD (mePPD; CAS no. 337906-36-2)
2	Bleaches	 persulfate salts: ammonium, APS, CAS no. 7727-54-0; potassium, PPS, CAS no. 7727-21-1; sodium, SPS, CAS no. 7775-27-1
3	Perms and relaxing substances	 salts and esters of thioglycolic acid: glyceryl thioglycolate (GMTG; CAS no. 30618-84-9), ammonium thioglycolate (ATG; CAS no. 5421-46-5)
		• cysteamine hydrochloride (cysteamine HCl; CAS no. 156-57-0)
4	Cosmetic glues	 2-hydroxyethyl methacrylate (HEMA; CAS no. 212-782-2) ethyl cyanoacrylate (ECY; CAS no. 7085-85-0)
5	Detergents	 cocamidopropyl betaine (CAPB; CAS no. 61789-40-0) sodium laureth sulfate (SLES; CAS no. 9004-82-4) cocamide diethanolamine (cocamide DEA; CAS no. 68603-42-9)
6	Film-forming	 polyvinylpyrrolidone (PVP; CAS no. 9003-39-8) polyvinylpyrrolidone (PVP) copolymers (CAS no. 28211-18-9)

In this paper, we describe a series of reviews conducted for this project. A review is a form of scientific publication. It summarizes the current state of research on a specific topic based on the published literature. Regarding the objective, different forms of reviews can be identified:

- Narrative reviews which synthesize primary studies and explore through description rather than statistics, usually not striving for a complete, balanced and quality-assessed evaluation of included literature.
- Rapid reviews which assess what is already known about a policy or practice issue by using systematic review methods to search and critically appraise existing research.
- Scoping reviews which preliminarily assess the potential size and scope of available research literature. Those reviews aim to identify the nature and extent of research evidence and to formulate specific questions which could be answered based on that evidence.
- Systematic reviews which use a pre-defined protocol aiming at including all relevant literature, systematically extracting and appraising the evidence contributed. If possible, quantitative summaries of any numerical outcomes (like risk or disease frequency) are provided in terms of meta-analyses to provide a more precise result.

Narrative, scoping and systematic reviews with meta-analyses where appropriate, were used in this project.

3.2 Main findings (executive summaries¹)

3.2.1 Skin

3.2.1.1 Hand eczema in hairdressers in Europe

Hairdressers are commonly affected by hand eczema due to skin hazardous exposure such as irritants and allergens in the work environment. This review aimed at giving an overview of the current scientific results concerning frequency expressed as percent diseased at a time point or a period of time and number of newly diseased during a defined period. Moreover, severity as well as the pattern of debut and the contribution of childhood eczema, also called atopic dermatitis on hand eczema in hairdressers, was evaluated. The results show that more than every third hairdresser acquires hand eczema at one point in life. In one year, one in five hairdressers had hand eczema. The lifetime frequency in fully trained hairdressers and hairdressing apprentices was almost identical. Hairdressers have a considerable increased risk of hand eczema compared to the general population due to occupational exposures.

Main results:

- More than one in three hairdressers in Europe develop hand eczema, which may affect their work ability.
- Most develop hand eczema already in apprenticeship, being potentially below 18 years of age.
- Occupational exposures to allergens and irritants are the main causes of hand eczema in hairdressers.

Key messages:

- A strategic and collective effort to prevent hand eczema in hairdressers is warranted.
- Prevention should already start during apprenticeship.
- The young age of hairdressers at the debut of occupational hand eczema and the long-term consequences emphasize the responsibility of relevant authorities to act.

Full article: Havmose MS, Kezic S, Uter W, Symanzik C, Hallmann S, Strahwald J, Weinert P, Macan M, Turk R, van der Molen HF, Babić Ž, Macan J, John SM, Johansen JD. Prevalence and incidence of hand eczema in hairdressers-A systematic review and meta-analysis of the published literature from 2000-2021. Contact Dermatitis. 2022 Apr;86(4):254-265. doi: 10.1111/cod.14048 https://onlinelibrary.wiley.com/doi/epdf/10.1111/cod.14048

¹ The summaries are divided according to affected organs, namely skin and respiratory, and reproductive effects.

3.2.1.2 Skin exposure to hair cosmetic products in hairdressers compared to consumers

Hairdressers are at high risk of developing occupational hand eczema. Opinions on the health and safety concerns of non-food consumer products, such as cosmetics and their ingredients, consider the exposure, that is, skin contact – if no adequate gloves are worn - of an 'average consumer', which does not account for the usually much higher occupational exposure to hair cosmetic products common in hairdressers. As a result, serious safety concerns owing to occupational exposures exist. The purpose of this review was to compare the frequency of exposure to various types of hair cosmetic products among hairdressers and consumers. The analyses showed that – dependent on the task – hairdressers were exposed 4 to up to 78 times more frequently than consumers regarding a wide spectrum of hair cosmetic products used in the daily working life ranging from shampoo, conditioner, oxidative and non-oxidative hair colours, and bleaching agents. The greatest difference in frequency of exposure was found for colouring hair with oxidative hair colour. To conclude, consumer usage frequency does not appear to be appropriate for representing hairdressers' exposure. Current standards do thereby not effectively address the occupational risks associated with hairdressers' use of cosmetics. The results of this study should lead to a reconsideration of current risk assessment procedures.

Main results:

- Hairdressers are exposed up to 78 times more than consumers to a wide spectrum of hair cosmetic products.
- The most significant difference in frequency of exposure between hairdressers and consumers pertains to colouring hair with oxidative hair colour.

Key messages

- Hairdressers must learn to use gloves consistently from the very beginning of apprenticeship.
- Adequate gloves need to be put at disposal by the employer.

Full article: Symanzik C, Johansen JD, Weinert P, et al. Differences between hairdressers and consumers in skin exposure to hair cosmetic products: A review. Contact Dermatitis. 2022 May;86(5):333-343. DOI: 10.1111/cod.14055. PMID: 35088418 https://onlinelibrary.wiley.com/doi/epdf/10.1111/cod.14055

3.2.1.3 Hand eczema caused by contact allergens in hair cosmetics

The burden of occupational hand eczema in hairdressers is high, and (partly strong) allergens abound in the hair cosmetic products they use. This paper reviewed published results concerning contact allergy to an indicative list of important active ingredients of hair cosmetics, namely, p-phenylenediamine (PPD, CAS no. 106-50-3), toluene-2,5-diamine (PTD, CAS no. 95-70-5), persulfates, mostly ammonium persulfate (APS, CAS no. 7727-54-0), glyceryl thioglycolate (GMTG, CAS no. 30618-84-9), and ammonium thioglycolate (ATG, CAS no. 5421-46-5). Where possible, a comparison was made between the frequency of contact allergy to one of the compounds seen in hairdressers and the frequency to that same compound seen in other, "control" patients. This comparison results in a "relative risk quotient", i.e. a factor by which the average skin allergy risk is increased among hairdressers. This relative risk quotient reported in literature ranged between 5.4 (PPD) and 3.4 (ATG). Compared to contact allergy, immediate-type hypersensitivity (allergic hives or possibly more severe, systemic reactions) are rare. To supplement above results, experimental results, exposures, and information from case reports were furthermore summarised. As a conclusion from this work, a clear excess risk of contact allergy in hairdressers is evident from the scientific literature published in the last 20 years. This should prompt further improvement of working conditions and product safety. Main result:

• Hairdressers have a 3 to 5-fold higher risk of acquiring a contact allergy compared to consumers.

Key messages

- Undertake risk assessment and evaluation of contact allergens specifically in the workplace context.
- Reduce exposure to contact allergens (use of gloves, substitution by other less hazardous chemicals when possible).
- Improve working conditions.
- Highlight allergy risks of active ingredients on products.

Full article: Uter W, Strahwald J, Hallmann S, Johansen D J, Havmose M, Kezic S, van der Molen H, Macan J, Babić Z, Franić Z, Macan M, Turk R, Symanzik C, Weinert P, John SM Systematic review on skin adverse effects of important hazardous hair cosmetic ingredients with a focus on hairdressers. Contact Dermatitis. Oct. 2022. DOI 10/1111 cod.14236 [epub ahead of print]

3.2.1.4 Contact allergy caused by 2-hydroxyethyl methacrylate (HEMA) and ethyl cyanoacrylate (ECA)

A further systematic review compiled scientific results regarding skin toxicity of 2hydroxyethyl methacrylate (HEMA; CAS no. 212-782-2) and ethyl cyanoacrylate (ECA; CAS no. 7085-85-0) contained in cosmetic glues used among hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications. The analysis of published results revealed that the risk for hairdressers and beauticians of developing contact allergy to HEMA compared to controls who are not hairdressers and beauticians appears to be 9-fold. Results in hairdressers for ECA are lacking, which can be regarded as a research gap, given the broad exposure via different cosmetic glues. Existing regulations do not sufficiently address the occupational risks for hairdressers and beauticians associated with the use of cosmetic substances containing acrylates and need to be reconsidered. This is already evident from the fact that the SCCS considers the use of HEMA too hazardous for consumers and has recommended that it be restricted to professionals (SCCS/1592/17) - the very group that, as mentioned above, certainly needs strict safety regulations in the workplace.

Main results:

- Hairdressers are much more exposed to hazardous substances such as 2-hydroxyethyl methacrylate (HEMA) and ethyl cyanoacrylate (ECA) contained in cosmetic glues than consumers.²
- Exposure risk of hairdressers and beauticians is 9-fold compared to consumers.

Key messages:

• Safety regulations urgently need to address occupational risks related to the use of acrylate-contained cosmetic substances for hairdressers and beauticians.

Full article: Symanzik C, Weinert P, Babić Ž, et al. Allergic contact dermatitis caused by 2-hydroxyethyl methacrylate and ethyl cyanoacrylate contained in cosmetic glues among hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications: A systematic review. Contact Dermatitis. 2022 Jun;86(6):480-492. DOI: 10.1111/cod.14056. PMID: 35088905. https://onlinelibrary.wiley.com/doi/epdf/10.1111/cod.14056

 $^{^{2}}$ A current paper by Aalto-Korte and Pesonen (2022) also accentuates that occupational exposure to acrylates contained in cosmetic glues might be relevant to a share of hairdressers working in the EU.

3.2.1.5 Contact allergy and skin irritation caused by selected hair cosmetic ingredients

This review focused on a set of further important ingredients of hair cosmetics, namely, cysteamine hydrochloride (cysteamine HCl; CAS no. 156-57-0), polyvinylpyrrolidone (PVP; CAS no. 9003-39-8), PVP copolymers (CAS no. 28211-18-9), sodium laureth sulfate (SLES; CAS no. 9004-82-4), cocamide diethanolamine (cocamide DEA; CAS no. 68603-42-9), and cocamidopropyl betaine (CAPB; CAS no. 61789-40-0). They are used as constituents in a wide array of products such as hair dyes, waving agents and shampoos. Summarizing the scientific results on contact allergy to CAPB, hairdressers have a 1.7-fold increased risk of developing contact allergy to CAPB (contained in shampoos and hair dyes) compared to controls who are not hairdressers. Only a few reports included cysteamine HCl, not enabling a similar comparison; however, hairdressers can be assumed to have a higher risk of becoming allergic to cysteamine HCl compared to a consumer because of their job responsibilities (higher frequency of performing permanent waving). Regarding cocamide DEA, the irritant potential of this surfactant should not be overlooked. Original articles for PVP, PVP copolymers, and SLES are lacking. This systematic review indicates that there is limited data available, except for CAPB, where a slightly increased risk of contact allergy has been found in hairdressers. However, virtually all these and similar substances exert some irritant effect on the skin. While for the "average consumer" such exposure may rarely cause skin problems, the cumulative dayby-day strain on hairdressers' hands – if not sufficiently covered by gloves and supported by the application of emollients - is a clear cause of irritant damage. Hairdressers therefore are at particular risk of becoming allergic to these or other more potent allergenic substances used in hair cosmetics. This should prompt a re-assessment of current risk management practices. Main results:

- Hairdressers have a 1.7-fold increased risk of developing contact allergy to CAPB (contained in shampoos and hair dyes) compared to controls who are not hairdressers.
- The cumulative day-by-day exposure of hairdressers to CAPB and other selected hair cosmetic ingredients leads to a skin damage, if not properly protected by appropriate gloves and use of emollients.

Key message:

• The cumulative irritation potential of detergents and other auxiliary substances must not be overlooked and needs more consideration in hand eczema risk management.

Full article: Symanzik, C.; Weinert, P.; Babić, Ž.; Hallmann, S.; Havmose, M.S.; Johansen, J.D.; Kezic, S.; Macan, M.; Macan, J.; Strahwald, J.; Turk, R.; van der Molen, H.F.; John, S.M.; Uter, W. Skin Toxicity of Selected Hair Cosmetic Ingredients: A Review Focusing on Hairdressers. *Int. J. Environ. Res. Public Health* 2022, *19*, 7588. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9265752/pdf/ijerph-19-07588.pdf

3.2.1.6 Other substances

There is clear evidence of an increased risk of sensitisation to the biocides Methylchloroisothiazolinone (MCI/MI) and Methyldibromo glutaronitrile (MDGBN), which are or were also used as preservatives in hair cosmetic products (see figures below). This is less clear for formaldehyde. The increase has been attributed in the underlying studies focusing on a comparison between female hairdressers and female clients/self-users to the fact that

(i) most hair cosmetics contain such preservatives, and

(ii) that exposure to these products, unprotected by gloves,

is much higher in hairdressers than in consumers. Thereby, the results with these auxiliary substances are a good illustration of the adverse effect of increased exposure by occupational use of the same (type of) products for which risk assessment had been performed just with a focus on the typical consumer exposure.

It can be concluded that hairdressers often work with unprotected hands and therefore have a higher exposure to these biocides. This interpretation fits with the figure regarding the exposure numbers. It shows that unprotected hands lead to a higher risk of sensitization to these excipients. Hence, preservatives in almost all hair cosmetics is an issue.

Figure 1: Summary of averaged risk estimates comparing contact allergy frequency in hairdressers vs. different controls in terms of a risk quotient (relative risk) shown on a logarithmic scale. Values above 1 indicate an increased, values below 1 a decreased risk in hairdressers.



(A) indicative broadly used preservatives and two main rubber allergens, see comments in the text.

(B) hair cosmetic ingredients in the focus of the present project; the two biased risk quotients are derived from studies using female clients with suspected contact allergy to hair cosmetics – meaning oxidative hair dye products in the vast majority – as a comparison group. As these

highly selected comparison patients have a very high likelihood of being diagnosed with contact allergy to hair dye ingredients, their resulting risk is very similar to that of hairdressers. Conversely, if a general comparison group is considered (top row for PPD), or if agents are concerned which are mainly used in (and on) the hand of professionals (GMTG, ATG, APS), the increased risk in hairdressers is apparent.

The increased risk concerning rubber allergens indicates - most likely - exposure via protective gloves and also stresses the importance of proper protective equipment, as gloves without rubber allergens do exist. A standard for gloves designed to protect hairdressers from chemicals in the work environment has recently been developed in the framework of the European Committee for Standardization (CEN). This needs to be implemented in practice.

3.2.2 Respiratory system

3.2.2.1 Exposure of hairdressers to airborne hazardous chemicals

Inhalational exposure to hazardous chemicals released during hairdressing activities from hair care products puts hairdressers at greater risk of adverse health effects. Safety assessment of hair products mainly focuses on consumers, but exposure for professional hairdressers might be substantially higher. Available research data on inhalation exposures of professional hairdressers were evaluated. The largest number of studies measured formaldehyde, ammonia, total volatile organic compounds (TVOC), and toluene. More than fifty other chemicals were measured scarcely, including various aromatic and aliphatic organic solvents, hydrogen peroxide, persulfate and particulate matter. The measured levels of formaldehyde, ammonia and TVOC exceeded current occupational exposure levels (OELs) or guidance levels in some studies. In hair salons in the EU only ammonia and TVOC exceeded OEL or guidance levels. Ammonia is released during bleaching, oxidative dyeing, or perm procedures, and can lead to

irritation of the skin, eyes, and respiratory system. Air concentrations measured in hairdressing salon air can induce irritation in the airway mucosa during and after bleaching operations, and it has been shown that hairdressers have a higher risk of developing irritation of the upper airways and asthma than persons not occupationally exposed to hairdressing chemicals, dominantly hair bleach. TVOC is commonly used in the assessment of indoor air quality, and their composition and toxicity vary. The major potential health effects from VOC include acute and chronic respiratory effects, allergies, neurological toxicity, damage to the liver and kidney, and some even reproductive effects, and carcinogenicity. There are no OELs for TVOC but exposure between 300 and 3000 μ g/m³ is associated with perceived discomfort as well as temporary symptoms of irritation in the eyes and the respiratory system. Hairdressers, especially if working in salons without local exhaust ventilation are exposed to the TVOC levels, which might lead to discomfort and adverse health effects.

Main results:

- Hairdressers are often simultaneously exposed to a wide spectrum of hazardous chemicals.
- The measured levels of ammonia and TVOC in the air of hairdressing salons in the EU exceeded OEL or guidance levels in some studies.
- Airborne concentrations of pollutants from hairdressing chemicals depend on salon characteristics such as ventilation and the number of customers, but also on used products, which are often country- or client-specific.

Key messages:

- Occupational inhalation exposure should be taken into account by safety regulations for hair care products.
- Indoor concentrations of chemicals in the hairdressing salons should be monitored and preventive measures such as proper ventilation systems should be taken if their levels are of concern.

Full article: Kezic S, Nunez R, Babić Z, Hallmann S, Havmose MS, Johansen J, John SM, Macan M, Symanzik C, Uter U, Weinert P, Turk R, Macan J and van der Molen H.F. Occupational exposure of hairdressers to airborne hazardous chemicals: a scoping review. Int J Environ Res Public Health. 2022;19(7):4176. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8998463/pdf/ijerph-19-04176.pdf

3.2.2.2 Respiratory toxicity of persulphate salts and their adverse effects on airways in hairdressers

Available literature on respiratory effects of persulfate salts (PS) or hair bleaches in hairdressers was reviewed. PS are indicated as the main cause of occupational rhinitis and asthma in hairdressers, and one of the leading causes of occupational asthma in some European countries. Bleaching products are the most important factor for the development of respiratory symptoms, a decline of the lung function, and eventually for leaving the hairdressing profession. Risk estimates from a good quality prospective study showed a higher risk for wheezing and breathlessness in hairdressers aged \geq 40 years than in matched controls, and a higher risk in hairdressers to develop respiratory symptoms from exposure to bleaching powder than controls. Pathophysiological mechanisms of the respiratory response to PS are not yet fully elucidated, but may include non-specific and specific immune responses, such as allergies.

Main results:

- Persulphate salts as a constituent of hair bleach are the main cause of occupational rhinitis and asthma in hairdressers and one of the leading causes of occupational asthma in some European countries.
- Bleaching products are indicated as the most important factor for development of respiratory symptoms, lung function decline, and leaving the hairdressing profession.

Key messages:

- Adopt harmonized OELs for persulphate salts at EU level.
- Use of safer bleach formulations (ready-to-use liquid, cream, paste).

Full article: Macan J., Babić Z., Hallmann S., Havmose M.S., Johansen J.D., John S.M., Macan M., Symanzik C., Uter W., Weinert P., van der Molen H.F., Kezic S., Turk R. (2022). Respiratory toxicity of persulphate salts and their adverse effects on airways in hairdressers: a systematic review. Int Arch Occup Environ Health (2022). https://doi.org/10.1007/s00420-022-01852-w

3.2.3 Systemic adverse health effects

3.2.3.1 Carcinogenicity and reproductive effects in hairdressers with a focus on permanent hair dyes

Hairdressers, an occupational population frequently exposed to hairdressing chemicals at work, are not sufficiently covered by regulatory risk assessment and seem to be at greater risk for systemic adverse effects than consumers. Exposure to chemicals *via* skin contact and inhalation not only causes local effects but can both result in the absorption of chemicals into the human organism. A systematic review of recent epidemiological studies investigating carcinogenic or reprotoxic effects among hairdressers was done.

Only one study showed that hairdressers have a nine times higher risk for bladder cancer than population-based controls, while other studies noted no increased risk for bladder and lung cancer and lymphoma. Regarding reprotoxic effects among numerous investigated outcomes (menstrual disorders, congenital malformations, fetal loss, small-for-gestational age, preterm infant, infertility), only the association with heart septal wall defects in newborns of fathers working as hairdressers was of borderline significance, and some indices of poor neonatal or maternal health were significantly associated with maternal occupation as a hairdresser (low Apgar score at delivery, pregnancy-induced hypertension, slowed labor with delayed delivery, postpartum hemorrhage). However, the absolute numbers of analyzed cases among hairdressers were very small which compromise the strength/validity of results. To conclude, there is no clear evidence that hairdressers are at an increased risk of carcinogenic or reprotoxic effects related to their trade. Yet, such risks cannot be clearly ruled out. Available scientific data cannot clearly separate hairdressing chemicals by their carcinogenic or reprotoxic potential, but permanent hair dyes are considered mainly responsible for these effects. The monograph of the International Agency for Research on Cancer (IARC) from 2010 made a clear distinction regarding the risk of carcinogenicity of hair dyes in hairdressers and consumers, classifying hairdressing occupation as probably carcinogenic to humans (Group 2A), while personal use of hair dyes is not classifiable as to its carcinogenicity to humans (Group 3).

3.2.3.2. Systemic adverse health effects of other substances

Formaldehyde is an often ingredient of various hair care products. It is a highly reactive, acutely toxic substance which can cause skin and respiratory tract irritation and corrosion, skin sensitisation, genotoxicity (DNA damage) and carcinogenicity. In the beauty salons, the level

of exposure depends upon the products used, stylist techniques, and ventilation. Formaldehyde is strictly regulated and severely restricted in the EU market but keratin-based hair straightening products may still expose hairdressers to concentrations above the current EU OEL of 370 μ g/m³. Recently adopted SCCS Scientific Advice further reduced levels of total free formaldehyde in cosmetic products that trigger the warning "contains formaldehyde" on the product label to only 0.001% (10 ppm) (SCCS, 2021).

Hairdressers using oxidative hair dyes are also exposed to resorcinol. Hair that had been rinsed after dyeing still contains traces of resorcinol. Traces of resorcinol were found in hand rinse samples of hairdressers after cutting newly dyed hair (Lind et al., 2005). In humans, exposure to resorcinol has been associated with thyroid effects, CNS disturbances, and red blood cell changes. Dermal sensitization has been well documented, but in practice it is rare. Recently, concerns have been raised over the effect of resorcinol on the endocrine system, especially the function of thyroid gland and possible adverse effects in pregnancy. However, biomonitoring study showed that hairdressers' exposure to resorcinol was at the same level as that of the reference population of occupationally non-exposed volunteers with values within the acceptable daily intake (ADI) established for resorcinol intake in general population by the European Food Safety Authority (EFSA) (Porras et al., 2018).

Thioglycolates are used in permanent waving products at concentrations up to 20%. Thioglycolic acid esters and salts can be irritating to the skin and eyes, and repeated exposures can cause skin sensitization. Indoor air concentrations of thioglycolic acid (TGA) measured in a beauty salon in Japan during perm treatment were much lower than the occupational safety guideline levels, suggesting that inhalation of airborne TGA is not important as a possible exposure route to hairdressers and customers (German MAK Werte, 2013).

Parabens are widely used as preservatives in cosmetics including hair care products, especially shampoos and conditioners. Scientific studies suggest that parabens, due to the estrogenic activity, can disrupt hormones in the body and harm fertility and reproductive organs, affect birth outcomes, and increase the risk of cancer. They can also cause skin irritation and allergy. Higher urinary levels of parabens were recorded in women working in beauty salons in comparison to non-exposed controls (Arfaenia et al., 2021). Specific data on paraben exposure in hairdressers are missing but the level of exposure is expected to decline due to legislative

restrictions and substitution with alternative preservatives such as 2-phenoxyethanol, isothiazolinones etc.

Main results:

- There is no clear scientific evidence that hairdressers are at increased risk of carcinogenic or reprotoxic effects related to their trade, but such risks cannot be clearly ruled out.
- In studies in which results suggest carcinogenic effects of hairdressing occupation, permanent hair dyes are considered mainly responsible, related to the development of bladder cancer.
- Recent literature is scarce due to the carcinogenic or reprotoxic effects of hairdressing chemicals, and more experimental and epidemiological studies are needed in this respect.

Key messages:

- Scarce literature on carcinogenic and reprotoxic effects implies precautionary principle should be applied aiming adequate skin and respiratory protection.
- Inventarisation and evaluation of risk associated with use of carcinogenic and reprotoxic chemicals should be performed in the workplace.
- Installation of appropriate ventilation systems alongside the introduction of appropriate ventilation procedures should be considered in hairdressing salons.
- Existing recommendations for adequate glove use in everyday working life should be emphasized and controlled.
- Preventive health-related contents should be conveyed in health education programs.

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4 Methodological Note

The following Methodological Note discusses how to put the obtained evidence into practice. It includes recommendations on risk assessment, preventive measures, and methodological suggestions.

4.1 Risk assessment

Hairdressers are at a significant risk of developing occupational hand eczema. Opinions elaborated by the SCCS and its predecessors on cosmetics and their ingredients consider the exposure of a "common consumer," which may not adequately account for professional exposure of hairdressers. As a result, substantial occupational safety problems exist. As our results show, hairdressers are – dependent on the task – exposed 4 to 78 times more than consumers to a wide spectrum of hair cosmetic products used in their daily working life, ranging from shampoos, conditioners, oxidative and non-oxidative hair colors, to bleaching agents (Symanzik et al., 2022a). The highest frequency was found for coloring hair with oxidative hair color (Figure 2).



Figure 2: Factor by which hairdressers are higher exposed than consumers (i.e., *exposure factor*) whilst conducting regular hairdressing activities; calculation formula: (frequency of exposure for hairdressers + frequency of exposure for consumers) / frequency of exposure for consumers; for full numbers on frequency of procedures using corresponding products and dose per area see Appendix II.

Hairdressers are, in addition, occasionally exposed to airborne chemicals released during hairdressing procedures in levels exceeding current OEL or guidance levels with irritating and

/or sensitizing effects on the respiratory system. Both dermal and inhalation exposure can result in the absorption of chemicals into the body with the potential for development of systemic adverse effects, like carcinogenicity and reproductive toxicity.

Hairdresser exposure does not appear to be represented by consumer usage frequency. The current regulations do not adequately address health risks (Table 2 and 3) linked with the occupational use of cosmetics by hairdressers. The outcomes of this study should prompt a rethinking of present risk assessment, which is based on consumer exposure.

The so-called "cocktail exposure", i.e. different allergens and/or skin irritants in one product (see Figure 3) - should be given greater consideration in risk assessment. Conversely, so-called "aggregate exposure", namely one allergen in different products, thus leading to a (much) higher exposure than assumed if considering just one product type (see Figure 3), is meanwhile considered to some extent in a revised version of quantitative risk assessment, albeit only for fragrance compounds. Similar considerations should be made for all toxicologically relevant substances.



Figure 3: Different factors with an impact on sensitization risk (Uter et al., 2013)

The below tables and figures present in summary the different risk exposure of hairdressers within the framework of their daily tasks such as washing hair, colouring hair and so forth.

Procedure with product types	Likely performed by consumers?†
1. Shampooing/washing hair using shampoo	yes, possibly daily
2. (Deep) Conditioning hair using hair conditioner	yes, possibly daily
3. Cutting wet hair i) without previously conducted colouring service and	i) no, ii) no
ii) after previously conducted colouring service	
4. Colouring hair i) with permanent/oxidative hair colour using 6-12%	i) yes, possibly monthly
hydrogen peroxide on the full head, ii) with semi-permanent oxidative	11), yes, possibly monthly iii) yes.
hair colour using 2-3% hydrogen peroxide or non-oxidative hair colour	possibly monthly
on the full head, iii) on the root/regrowth only with oxidative/non-	
oxidative hair colours according to previous treatment	
5. Highlighting the hair (mostly using bleach with 6-9% hydrogen	no
peroxide) and lowlighting the hair (mostly using oxidative hair colour	
with 6% hydrogen peroxide) using (aluminium) foil	
6. Highlighting the hair (mostly using bleach with 6-9% hydrogen	no
peroxide) and lowlighting (mostly using oxidative hair colour with 6%	
hydrogen peroxide) the hair using a cap	
7. Bleaching the hair with bleach using mostly 6-9% hydrogen peroxide	rarely
on the full head	
8. Perming the hair using waving/perming lotions (acid, alkaline, and	no
exothermic perms)	
9. Colouring eyelashes and/or eyebrows with oxidative hair colour using	highly unlikely
mostly 3% hydrogen peroxide	

Table 2: Identified procedures alongside with concomitantly used product types

†categories: yes, possibly daily; yes, possibly monthly; rarely; highly unlikely; no

In May 2022, the European Partnership for the Assessment of Risks from Chemicals (PARC) was launched with a view to developing next-generation chemical risk assessment, incorporating both human health and the environment in a "One Health" approach. It will help support the European Union's Chemicals Strategy for Sustainability and the European Green Deal's "zero pollution" ambition. Bringing together nearly 200 partners from 28 countries as well as EU agencies, PARC is coordinated by the ANSES (Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail; French Agency for Food, Environmental and Occupational Health & Safety) with funding from the European Commission's Horizon Europe research and innovation framework programme and the partnership participants. An important goal of this collaboration is to provide a common strategy for risk assessment of skin allergens, which does not exist currently. The problem of

assessing mixtures is dealt with in several work packages (https://www.anses.fr/en/content/launch-european-research-and-innovation-parc-programmeimprove-chemical-risk-assessment). It will be important that stakeholders such as the social partners of the hairdressing trade support this process and its goals. Submitting the Medical Reference Document (MRD) to the PARC coordinators at ANSES could be an initial step for a dialogue where the health and safety of hairdressers are put into focus. Table 3: Additional sources of exposure (extract) to potentially harmful substances in the hairdressing trade alongside corresponding tasks, also involving cosmetic product categories not for use on hair

Product	Potentially harmful substances (extract)	Exposure route	Are gloves usually worn?	Comment
eyelash glue	acrylates	dermal, respiratory	no	For some make-up services eyelash extensions are used. The eyelash glue is placed on the back of the hand and the eyelash extension is dipped into the glue. The remaining eyelash glue (dried residue) may only be removed at the end of the working day. Dermal and respiratory effects of eyelash glues have already been reported. (Lindström et al., 2013; Pesonen et al., 2016)
nail glue	acrylates	dermal, respiratory	no	Press-on-nails or nail art decorations (e.g. rhinestones) are applied with nail glue within the course of conducting manicures. The nail glue may get on the fingers of the hairdresser and only be removed at the end of the working day. Dermal and respiratory effects of nail glues have already been reported. ^(Sauni et l., 2008; Jurado-Palomo et al., 2008; Lazarov, 2017)
hair extension glue	acrylates, latex	dermal, respiratory	no	A variation of hair extension glues is used to install hair extensions. Allergic reactions against hair extension glues have already been reported. ^(Burla et al., 2002; Cogen et al., 2002; Wakelin et al., 2002) The mentioned glues range from liquid delivery forms to adhesive strips (so-called tapes). Whilst installing hair extensions, gloves are regularly not worn exposing the hairdressers to the glues for a considerable amount of time during conducting the service on the client. Glue residue might remain on the hands until they are thoroughly cleaned off at the end of the working day.
hot wax, sugaring paste	colophony, cera alba, fragrances	dermal	no	Depilation of undesired body hair (e.g. facial hair in women) may be removed by hairdressers using hot wax or sugaring paste. Whilst depilating the hair, the hot wax/sugaring paste can get on the hands of the hairdresser and needs to dry before it can be removed. Dermal effects of hot wax/sugaring paste have already been reported. ^(Nanyan et al., 2019; de Argila et al., 1996; Quain et al., 2007)
hair styling and setting products (e.g. hairspray)	aerosols, resins, fragrances	dermal, respiratory	no	Styling products (e.g. hair gels) are applied by the hairdresser without gloves and the hands are usually not washed until the service is finished. In order not to get setting products (e.g. hairspray) into the customers' face, the hairdresser protects it using their own hand whilst spraying with the other getting the hairspray on the protecting hand. Dermal and respiratory effects of hairsprays have already been reported. ^(Heine et al., 1990; Borum et al., 1979)
metal tools/objects (e.g. tweezers, crochet hooks)	nickel and/or cobalt	dermal	no	Tweezers are used to pluck eyebrows and to remove undesired facial hair. A nickel and cobalt release (and also a co-release of both) from tweezers has already been reported. ^(Symanzik et al., 2019; Symanzik et al., 2021) Crochet hooks are used for highlighting/lowlighting the hair using a cap. A nickel release from tweezers in the hairdressing trade has already been reported. ^(Symanzik et al., 2021; Thyssen et al., 2009)

4.2 Prevention

In health care, prevention is a generic term for targeted measures and activities to avoid diseases or damage to health, to reduce the risk of the disease or to delay its occurrence. The so-called "STOP principle" is applied in occupational health and safety (see also Appendix III). It defines the hierarchy of protective measures and groups them. The abbreviation **STOP** stands for

- Substitution (e.g., GMTG banned in perming solutions and replaced by other agents by means of a national regulation)
- Technical measures (e.g., suitable room ventilation for hairdressing salons)
- Organizational measures (e.g., to ensure that unavoidable wet work is distributed as fair as possible among several employees in order to reduce exposure for the individual)
- Personal measures (e.g., supply and use of suitable protective gloves)

For primary prevention (i.e., measures to prevent or delay onset of a disease), a risk assessment and evaluation should be performed at each hair salon. Based on the identified risk for hazardous chemical substances, the STOP principle can be used to select and implement feasible preventive measures together with employers, workers and health professionals. Several risk assessment tools are already available, e.g. a tool provided by EU OSHA (<u>https://oiraproject.eu/sv/oira-tools/hairdressers</u>). Secondary prevention aims to prevent disease progression. It intervenes in existing risk situations and tries to avert them and reduce the consequences of the disease. Tertiary prevention focuses on restoring health to existing disease.

Within the framework of the COST Action StanDerm (TD 1206), minimum standards on prevention, diagnosis and treatment of occupational and work-related diseases in Europe were defined. It states that in order to reduce the burden of occupational skin diseases, equivalent standards of primary, secondary and tertiary prevention need to be established in Europe, with a focus on communicating and disseminating information to workers at risk. This was recently underlined by the current *European guidelines for diagnosis, prevention, and treatment of hand eczema* (Thyssen et al., 2021). In the context of the new EU strategic framework on safety and health at work 2021-2027, in which improving prevention of work-related diseases is one of the three key objectives with a focus on "updating the methodology for addressing hazardous substances to identify further efficiencies in establishing OSH limit values", action must be taken to improve the health and safety of hairdressers. The main priorities are defined as:

- 1. Anticipation and management of change against the background of ecological, digital and demographic change.
- Improving the prevention of work-related accidents and diseases with the aim of a "Vision Zero" approach to work-related fatalities.
- 3. Increasing preparedness for current and future health crises.

Based on the results of this study, the following chapters present preventive measures that should be considered for implementation in the hairdressing trade. Examples from different EU countries are provided to illustrate successful measures.

4.2.1 Skin

Prevention of skin diseases is important, even in early career stages

Most hairdressers have onset of hand eczema during apprenticeship or shortly after graduating, which is why primary prevention in the beginning of the apprenticeship is necessary. The consistent use of preventive measures is already necessary in early career stages, in which the learning contents can be taught within vocational schools. Further, early diagnosis and intervention are needed (Alfonso et al., 2017). In Denmark, an evidence-based skin protection program was implemented nationwide in 2011 in all Danish hairdressing vocational schools (see Figure 4). A regular update of knowledge by means of a refresher training should be facilitated by the employer. Within continuing education (e.g. German hairdressing master course "Friseurmeister"), implementation of these measures should be stressed again.

Box 1 Special skin protection program for hairdressers
Use gloves when you wash, dye, bleach, and perm ¹⁰ ²⁴ Cut before you dye the hair ²⁵ ²⁶ Mix in a separate, ventilated cabinet ²⁷ Disposable gloves must be clean, new, and dry ²⁸ Never reuse disposable gloves ²⁸ Use cotton gloves underneath protective gloves ²⁹ Use gloves for as long as nescessary, but as shortly as possible ^{29 30} Use an unscented, lipid rich moisturizer ^{31–33} Do not wear rings when you work ³⁴
Use gloves when doing wet work in your spare time ³³ Use warm gloves outside when it's cold ³⁶

Figure 4: Evidence based skin protection program implemented in Danish hairdressing vocational schools (Bregnhøj et al., 2012).

In 2015, the Danish executive order on hairdressing vocational training was updated making skin protection training mandatory. Apprentices were further required to pass a written exam on the skin protection curriculum to continue apprenticeship and be able to use personal protective equipment in accordance with the skin protection training at the final apprenticeship exam. Hairdressers who graduate after implementing the skin protection program are more compliant with personal protective equipment and have half the risk of developing occupational hand eczema. It should be considered to implement similar mandatory educational programs across the EU.

Occupational dermatoses require early diagnosis and intervention

In Germany, a multi-disciplinary intervention program has been in place for decades with a focus on occupational contact dermatitis, and with proven success in hairdressers. As part of the German intervention program, it is established that at early signs of hand eczema/contact dermatitis, hairdressers (as any other worker) have quick and easy access to a dermatologist, for diagnosis and treatment. It is well known that identifying allergies and subsequently avoiding them improves the chances of recovery and the possibility of remaining in employment. This is supplemented by educational events in skin protection (SIP) and more advanced seminars, if the disease is severe (TIP), when the hairdresser/worker is admitted as in-patient for treatment and specific education. These programs (SIP and TIP) have proven very successful and have been copied by other countries. Recently, it has been proposed that similar SIP and TIP programmes be implemented across the EU.

Personal protection is a relevant measure in hairdressers

The appropriate use of gloves must be considered as one of the most important personal protection measures for hairdressers. Gloves must be i) available, ii) clean, and iii) single use. The right material provides protection against penetration of substances of toxicological concern (new CEN Standard in preparation) and with low or no allergenic rubber chemicals. In addition, hairdressers need to know how to use the gloves properly and how to take them off safely (Figure 5). Hairdressers often do not use gloves for activities such as washing their hair because they subjectively have limited tactility. It is also known that hairdressers reuse already worn gloves, sometimes even putting them inside out. This highlights the need for proper

education on this topic; no surgeon would ever perform surgery without gloves. Using gloves should be a natural habit in hairdressing, like putting on a seat belt in a car.



Figure 5: How to take off protective gloves. It is important to take off protective gloves correctly to avoid contamination of the hands. Hairdressers need education on this in order to enable them to sufficiently protect themselves. <u>https://www.videncenterforallergi.dk/allergi-og-eksem/haandeksem/forebyggelse-med-handsker/korrekt-aftagning-af-engangshandsker/</u>

Wet work: a pivotal factor in the genesis of occupational hand eczema

Wet work entails tasks where employees:

- have their hands regularly submerged in water for longer than two hours each day
- must regularly (e.g., 20 or more times per day) or thoroughly wash their hands
- wear waterproof gloves; if no effective steps are made to allow the skin to recover, the time spent wearing such gloves is added to the time spent in a damp environment.

The water, detergents, water-soluble irritants, soils that are specific to the various occupations, and sometimes mechanical forces are irritating factors within the generic concept of wet labor (e.g., rubbing while cleaning or hand-washing). Although water and occlusion by themselves are just mild irritants, they work together to intensify the irritating effects of detergents and other product ingredients.

More emphasis should be placed on initiatives to reduce wet work for individual hairdressers, as this is a major risk factor for the development of hand eczema. This could be done by

organizing work tasks, focusing on the use of protective gloves for wet work and caps per working day.

Risk assessment of hair cosmetic products at EU level needs urgent re-evaluation

As identified in this study, improved risk assessment concerning skin sensitizers in products would be a major step forward, taking into account the increased exposure of hairdressers compared to consumers. Only then will it be possible to acknowledge the actual exposure hairdressers have in daily working life. This will also be the adequate starting point for specifically tailoring preventive measures (risk management). Based on the results of this study, this would lead to an overall safer use of potential skin sensitizers, which would be an important part of primary as well as secondary and tertiary prevention. As mentioned above (p.23), support from the hairdressing trade's social partners is pivotal for hairdressers to benefit from the initiatives under the European Partnership for the Assessment of Risks from Chemicals (PARC).

In conclusion, the consistent application of preventive measures is already necessary in the early vocational phases, when the learning contents can be taught in vocational schools. With such early training and evidently full support from the salon owners, wearing gloves could become an automatism, like putting on a seatbelt in a car. Early diagnosis and intervention are furthermore needed. A regular update of knowledge by means of a refresher training should be facilitated by the employer. Within the framework of continuing education (e.g. German hairdressing master course "Friseurmeister"), the implementation of these measures should be repeated.

4.2.2 Airways

Increasing awareness on inhalation hazard avoidance is a prerequisite for reducing inhalation exposure and improving respiratory health in hairdressing workers. Educational programs focused on safety and health at work should be implemented from vocational schools to ongoing workers' training. They should include primarily technical and organizational measures. Technical measures include installation of adequate ventilation with external exhaust away from workers breathing zone. Exposure pathways may vary significantly based on the type of services provided, and monitoring of salon air contamination may be necessary to establish the risk of excessive exposure in order to address the highest level of the most hazardous airborne chemicals and effectively plan the ventilation and exhaust system. Careful workspace organization enabling the use of selected tools, like flat iron only in well ventilated areas and providing the nail bars with additional local ventilation is recommended. Good work hygiene is also important and paying attention to closing the containers of hair products when not in use, avoiding contamination of surfaces and tools and proper disposal of hazardous waste are simple and effective chemical safety measures. Product substitution should be always considered by choosing, for example, low VOC formulas, paste or liquid formulations of hair bleach instead of powder, formaldehyde-free hair straighteners and pump sprays rather than aerosols. Face masks are rarely worn by salon workers regarding protection from chemicals, however regular use of protective gloves is shown to reduce the risk of both skin and respiratory sensitization to chemicals such as hair bleaches. Suitable safety manuals available at the workplace may also be useful.

4.2.3 General toxicity

Skin contact and inhalation of chemicals used professionally by hairdressers results in absorption into the human organism and a possible risk of acute and chronic systemic health effects. Consequently, both prevention of skin and inhalation exposure, as already described, reduces the risk of not only local, but also systemic toxic effects. Skin damaged by irritation or allergic reaction is more permeable for exogenous substances, which enter the circulation, disseminate to tissues and organs where they can accumulate and interfere with normal body functions. Combined exposure to chemical mixtures in hair salons is an additional health risk, especially for vulnerable populations, such as women of reproductive age, pregnant and breastfeeding workers or apprentices and young workers, where a careful distribution of tasks also helps minimizing the length and intensity of exposure.

4.3 Methodological suggestions

In the future, standard research methods for the evaluation of the impact of cosmetic substances on the health of hairdressers are necessary because the safety of hair cosmetic products is a mandatory regulatory requirement.

Development, validation and implementation of new approach methodologies (NAM) are needed

In recent years, an increasing number of new approach methodologies (NAM) for registration and risk assessment of cosmetic products and cosmetic ingredients has been developed, validated and adopted as test guidelines (Kim et al., 2021). NAMs are regarded as an important tool in the exposure-led and hypothesis-driven risk assessment approach (Next Generation Risk Assessment, NGRA) which was recently proposed for safety assessment of cosmetics.

NAMs include in *vitro, ex vivo, in chemico* (based on chemical reactivity), and *in silico* (computational) methods, read-across, as well as combinations thereof. While *in vitro* testing has already widely been used e.g. to evaluate acute toxicity, ocular irritation, skin irritation, skin sensitization, dermal absorption, genotoxicity, and carcinogenicity, new approaches which do not include experimental testing are still being developed and evaluated. The safety evaluation of cosmetic ingredients offers a greater flexibility as, on a case-by-case basis, the SCCS may accept new testing methods and approaches that are scientifically valid, but that are not formally validated. In Figure 6 an overview of new risk assessment approaches for cosmetic ingredients is given whereas both hazard identification and exposure assessment are considered to enable risk characterization (Kim et al., 2021).



Figure 6: Proposed methods for new approach methodologies (NAMs) (adapted from Kim et al., 2021). PBPK, physiologically-based pharmacokinetics.

The new toxicity assessment is shifting from an end-point based strategy towards more mechanism- and exposure-based approaches, which provide more insight in the pathways underlying toxic effects in humans and integrate multiple data types into one assessment (Arnesdotter et al., 2021). Examples of NAMs, which are not based on experimental studies, include read-across and *in silico* methods. Read-across methods are used for predicting the toxicity for one substance by using the knowledge and experience of experts on the data from (an)other structurally-related analogue(s). The European Chemicals Agency (ECHA) published a "Read-Across Assessment Framework (RAAF)" (ECHA, 2017) and a recent publication of SCCS introduced and suggested the read-across method for safety assessment (SCCS, 2020a). It should be noted, however, that read-across should be carried out using appropriate tools that allow an objective selection of analogues and the definition of similarity between the parent compound and the analogues (Schultz et al., 2017). Furthermore, read-across approaches still have challenges before more complex endpoints, e.g. repeated dose systemic toxicity and developmental and reproductive toxicity, can be appropriately assessed (Arnesdotter et al., 2021).

QSAR (Quantitative Structure-Activity Relationships) computational models are based upon the principle that a molecular descriptive or structural feature of a substance is related to a quantitative measure of a property such as a toxicological endpoint. The European Chemicals Agency considered QSAR predictions are not reliable for complex toxicological endpoints, unless there is additional supporting evidence covering all elements for that toxicological property (ECHA, 2017a). Although this opinion of ECHA is also shared by the SCCS, the recent Notes of Guidance note that some of the currently available high-quality models and tools can provide additional supporting evidence that can be used as part of the weight of evidence for risk assessment of cosmetic ingredients (SCCS, 2021).

In addition to NAMs for hazard identification, several QSAR's and PBK (physiologically based kinetic) models have been developed for the assessment of dermal or combined dermal and inhalation exposure, which might be of relevance for hairdressers as many chemicals in hair care products can (simultaneously) be absorbed through the skin and lungs. For the safety assessment of cosmetic ingredients, the concept of margin of internal exposure (MOIE) has been explored which uses an integrated modeling approach (PBK and QSAR modeling) to estimate internal exposures, thus facilitating route-to-route extrapolation (Bessems et al., 2017). This concept however has not been taken up in the SCCS Notes of Guidance (SCCS, 2021). At present, data on dermal absorption to evaluate the safety of cosmetic ingredients is still based on *in vitro* test methods.

Further, individual exposure of professional hairdressers should be better characterized, as it is crucial for health risk assessment and implementation of prevention measures. Besides routine hygienic measurements aimed at measurement of specific compound(s), non-targeted mass spectrometry analysis might be useful for identification of suspected chemicals. There are several models intended mainly to predict consumer exposure (ConsExpo, PACEM), however they are not evaluated for occupational exposure. Biomonitoring (BM) might play an important role for exposure assessment in hairdressers as it provides information on dermal and inhalation exposure, which both occur during hairdressing tasks. BM is based on the measurement of toxic chemicals or their metabolites in biological substances, usually urine, blood or exhaled air. To implement BM in occupational practice, efforts for the legal enforcement of biological limit values in the EU should be advanced. Furthermore, guidance to help employers set up a BM programme as part of their overall approach to chemical risk management at the workplace should be developed.

Table 4 summarizes recommendations or rather future action points for consideration concerning specific groups of substances.

Product category	Substances	Relevant health effects	Route of exposure (skin, airways, systemic absorption)	Inhalational occupational exposure levels (OELs)	Prioritisation*		
					Skin	Respiratory/ systemic	
Bleaches	Persulfate salts: ammonium, potassium, sodium	skin, airways and eye irritation, skin and respiratory sensitization	skin, airways	0.1 mg/m ³ (ACGIH)		а	
hair dyes, colorants	Toluene-2, 5- diamine (sulfate)	eye irritation, skin sensitization, hepatotoxicity		n/a		b	
	<i>p</i> -Phenylen- ediamine	skin sensitization, myotoxicity	skin, airways,	0.1 mg/m ³ (US OSHA)		b	
	2-Methoxymethyl- <i>p</i> - phenylenediamine (ME-PPD)	skin sensitization	systemic absorption	n/a		с	
Cosmetic glues	2-Hydroxyethyl methacrylate (HEMA)	eye irritation, skin sensitization, renal toxicity	skin	n/a		с	
Perms and relaxing substances	Cysteamine hydrochloride (cysteamine-HCI)	skin and respiratory irritation, skin sensitization	skin, airways, systemic toxicity	n/a		d	
	Glyceryl thioglycolate		skin	2 mg thioglycolate/m ³		e	

Table 4: Synopsis of results: The most relevant product groups to focus on to improve health and safety in the hairdressing trade

		skin, airways and eye	airways, systemic absorption	(DFG MAK values) 4 mg/m ³ as	
	Ammonium thioglycolate	irritation, skin sensitization		TGA(NIOSH) n/a	e
Detergents	Cocamide DEA Cocamido propylbetaine	skin and eye irritation, skin sensitization, hepatorenal toxicity, carcinogenicity (IARC 2B), Annex III/60 Cos. Reg. skin and eye irritation, skin sensitization	skin, systemic absorption	n/a n/a	d
			skin		
	Sodium laureth sulfate	skin and eye irritation	skin	n/a	
Film- forming	PVP-copolymers (Polyvinylpyrrolid one (PVP))	eye irritation, skin sensitization	skin	n/a	

* This column prioritizes by colors the findings of this study which has identified the most relevant product groups that need to be taken into focus for improving health and safety in hairdressing, separately for respiratory/systemic and skin effects. Accordingly, re-consideration of risk assessment is pivotal, also as a basis for adequate prevention. **Red** marks highest urgency, **orange** marks urgency, and **green** marks the lesser urgent need for action.

a: setting of EU OELs; **b:** studies on individual exposure and CMR potential needed; **c:** studies on individual exposure needed; **d:** studies on individual exposure and toxicokinetics needed; **e:** studies on internal exposure and reprotoxic effects needed, explore setting of biological exposure limits; **n/a:** not available (quantitative risk assessment regarding inhalation exposure is currently not possible)

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6 Appendices

6.1	Appendix	I: Plots	comparing	hairdressers	to consumers
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MCI/MI	Haird	esser	Cor	itrol			MDBGN	Haird	resser	Сон	ntrol		
¶st author, year	pos.	neg.	pos.	neg.		Risk Ratio [95% CI]	1st author, year	pos.	neg.	pos.	neg.		Risk Ratio [95% CI]
Uter, 2003	30	854	21	1196		1.97 [1.13, 3.41]	Uter, 2003	61	823	33	1184	-	2.54 [1.68, 3.85]
Uter, 2007	17	423	12	697	-	2.28 [1.10, 4.73]	Uter, 2007	26	419	28	686	÷	1.49 [0.89, 2.51]
Uter, 2014	39	667	43	1863	· • ·	2.45 [1.60, 3.74]	Uter, 2014	14	511	24	1350		1.53 [0.80, 2.93]
RE Model (Q = 0.	38, df =	2, p = 0.	83; I ² = 0.	0%, τ ² = 0.0	0) +	2.26 [1.67, 3.07]	RE Model (Q = 3.	15, df =	2, p = 0.	21; I ² = 3!	9.4%, τ ² = 0	.05)	1.88 [1.28, 2.76]
(A)				0.25 R	1 4 isk Ratio (log sca	16 le)	(B)				0.25 F	1 4 Risk Ratio (log scal	16 e)
Faldehyde	Hair	dresser	Ce	ontrol			Thiuram mix	Hair	iresser	Co	ntrol		
1st author, year	pos	, neg.	pos.	neg.		Risk Ratio [95% CI]	1st author, year	pos	. neg.	pos.	neg.		Risk Ratio [95% CI]
Uter, 2003	10	874	17	1200	-	0.81 [0.37, 1.76]	Uter, 2003	21	863	18	1199		1.61 [0.86, 3.00]
Uter, 2007	13	421	6	703		3.54 [1.36, 9.24]	Uter, 2007	12	419	10	700		1.98 [0.86, 4.54]
Uter, 2014	9	695	16	1882		1.52 [0.67, 3.42]	Uter, 2014	20	678	37	1868		1.48 [0.86, 2.52]
RE Model (Q =	5.49, df :	= 2, p = (0.06; l ² = (\$4.2%, τ ² = Γ	0.33)	1.57 [0.69, 3.55]	RE Model (Q = 0).34, df =	= 2, p = 0	1.85; I ² = 0	.0%, τ ² = 0.	00)	1.61 [1.12, 2.32]
(C)				0.25	1 4 Risk Ratio (log so	16 ale)	(D)				0.25 F	1 4 Risk Ratio (log scal	16 e)

Appendix I: eight plots summarizing and pooling results from the three successive IVDK studies comparing female hairdressers and female clients (i.e., female patients in whom hair cosmetics had been identified as likely cause of their contact dermatitis):

(A) Methylchloroisoziazolinone/methylisothiazolinone (MCI/MI);

(**B**) Methyldibromo glutaronitrile (MDBGN) or MDBGN with phenoxyethanol (PE) 1:4, the latter tested during the initial period;

(C) Formaldehyde;

(**D**) Thiuram mix, i.e., tetramethylthiuram monosulfide, tetraethylthiuramdisulfide (Disulfiram), tetramethylthiuramdisulfide, dipentamethylene thiuramdisulfide;



(E) 2-Mercaptobenzothiazole (MBT);

(F) Fragrance mix I, i.e., cinnamyl alcohol, cinnamal, hydroxycitronellal, amyl cinnamal, geraniol, eugenol,

isoeugenol, Evernia prunastri (Oakmoss absolute)

(G) Fragrance mix II, i.e., hexyl cinnamic aldehyde, Hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC), farnesol, coumarin, citral, citronellol;

(H) Hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC).

6.2 Appendix II: Data for the exposure factor by which hairdressers are higher exposed as consumers

Table 6: Characteristics of exposures in hairdressers and consumers. Procedures including used products alongside with the dose per area and the exposure factor by which hairdressers are higher exposed than consumers

	Hairdressers			Consumers		Exposure factor
Exposure	Frequency of procedures using corresponding products (median)	Regular glove wearing (%)†	Dose per area (mg/cm²/day) ‡	Frequency of procedures using corresponding products (median)§	Dose per area (mg/cm²/day)‡	
Shampooing/washing the hair with shampoo	5 - 12 times/day ^{Uter et al. 1998,} Lysdal et al. 2012	23.9	60.81395 - 145.95349	1 time/day	18.03448	6 - 13
Deep conditioning the hair with hair conditioner	1 - 5 times/day ^{Uter et al.} 1998, Lysdal et al. 2012	11.5 (+head massage: 8.4)	4.55814 - 22.79070	0.28/day	1.89241	5 - 19
Colouring hair with permanent/oxidative hair colour using 6-12% hydrogen peroxide (full head)	30.6 - 76.6 times/month ^{Uter} et al. 1998, Lysdal et al. 2012, Leino et al. 1998	95.2	0.24689 - 1.54711	1 time/month	0.00039	32 - 78
Colouring hair with semi-permanent oxidative hair colour using 2-3% hydrogen peroxide or non-oxidative hair colour (full head)	3 times/week ^{Lysdal et al. 2012}	95.2§	0.01465	1 time/week§	0.00241	4
Colouring hair (root/regrowth only) using oxidative/non-oxidative hair colours according to previous treatment	11.5 times/month ^{Lysdal et al.} 2012	95.2§	0.01220	1 time/month¶	0.00014	13
Bleaching the hair with bleach using mostly using 6-9% hydrogen peroxide (full head)	7.6 - 47.9 times/month ^{Uter et} al. 1998, Lysdal et al. 2012, Leino et al. 1998	77.9	0.01523 - 0.09599	1 time/month¶	0.00039	9 - 49

[†]data taken from Uter *et al.* (1998)¹⁰; [‡] calculation formula: (amount / skin surface area) x daily exposure frequency, the amount is taken from the SCCS Notes of Guidance (NoG) for the testing of cosmetic ingredients and their safety, 11th revision⁷ which refer back to Hall et al. (2007)⁹, Hall et al. (2011)⁸, Colipa 16.01.97 BB-97/007¹¹, and the Scientific Committee on Cosmetic products and Non-Food Products intended for consumers (SCCNFP) SCCNFP/0321/00¹², data on the skin surface area (SSA) is taken from the NoG⁷ which refer back to Bremmer et al. $(2006)^{13}$ and Bremmer et al. $(2006)^{14}$, for hairdressers the SSA of the hands (860cm²) and for consumers the SSA of $\frac{1}{2}$ head (580cm²) was considered; § data taken from the NoG⁷; ¶ factor by which hairdressers are higher exposed as consumers, calculation formula: (frequency of exposure for hairdressers + frequency of exposure for consumers) / frequency of exposure for consumers; day, 8 working hours; month, 21 working days; week, 5 working days

the studied cohort consists of hairdressers; the study cohort consists of adolescents; & water exposure is studied rather than wet work; h, hour; s, seconds

6.3 Appendix III: General preventive measures and STOP principle

General preventive measures encompass (*excerpt from TRGS 530, item 5*):

(1) When avoiding the exposure of workers to hazardous substances (in particular sensitising substances) and to damp work, technical protective measures have priority over organisational measures, which in turn have priority over personal protective measures. To avoid skin and respiratory contacts, all technical and organisational possibilities must be used.

(2) For hygienic reasons, employees shall not eat, drink or smoke in workrooms.

(3) Arm or hand jewellery must not be worn at work, as underneath the jewellery the effects of moisture or chemicals of pathological skin changes is particularly favoured.

(4) Care shall be taken to ensure that aqueous solutions containing substances or preparations

do not dry on the skin, but are washed off, as the concentration of pollutants on the skin rises sharply as the water evaporates.

(5) The use of used customer towels to dry hands is to be prohibited, as contamination with substances hazardous to the skin are not readily recognisable.

Examples of measures according to the STOP principle (substitution, technical, organizational, personal) are displayed in Table 7.

Table 7: Preventive measures according to the so-called STOF	P principle (substitution, technical, organizational, personal)
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Substitution	Technical measures	Organizational measures	Personal measures
(1) GMTG was banned and has	(1) Suitable room ventilation must	(1) The employer shall take	(1) Suitable protective gloves must
been replaced by other waving	be provided for hairdressing salons.	organisational measures to ensure	be made available to employees for
agents. This reduced GMTG	Provided that the risk assessment	that unavoidable wet work (e.g.	the following activities, and must be
sensitization in hairdressers.	does not reveal any other	washing hair, cutting wet hair, but	worn by the employees:
(2) Dusting hair bleaching	indications, the employer can	also the	- Head massage with hair and scalp
powders were substituted by	assume that a fresh air volume of	gloves) is distributed as far as	care products applied,
dust-free bleaching powders or	100 m 3 /h per employee is	possible among several employees	- colouring, tinting and bleaching -
bleaching creams. This	sufficient. Those involved in	in order to reduce exposure for the	including checking the result,
	hairdressing work are then decisive	individual. This applies to all	emulsifying and rinsing,

reduced respiratory exposure	for the design of the ventilation.	employees to the same extent, i.e.	- perming - including trial wrapping
to those dusts.	Ventilation can be achieved by	also to trainees and unskilled	- and fixing,
	exhaust fans, natural cross-	workers.	- preparation, mixing and decanting
	ventilation or a ventilation and air	(2) As a rule, it can be achieved	of hazardous substances,
	conditioning system and must be	through suitable organisation that	- hair washing,
	guaranteed at all times, even in	the wet work required in the salon is	- wet cleaning or disinfection of
	winter. and must be guaranteed at	below 4 hours per day for all	work equipment, devices, tools and
	all times, i.e. also in winter.	employees. The measures necessary	rooms
	(2) For mixing and decanting	for this are to be taken. In addition,	(2) When selecting and using
	work, specially designated	efforts should be made to limit the	protective gloves, the following
	workplaces shall be provided. The	duration of regular daily wet work to	criteria must be observed:
	work surface must be made of	less than 2 hours.	- They must be sufficiently
	liquid-tight, washable material. If	(3) The following applies when	impervious to hairdressing
	only processes are used for mixing	working with spray cans:	chemicals. This means protection
	and decanting operations which do	- Follow the instructions for use	against low chemical hazards (see
	not release hazardous gases,	printed on the spray can or enclosed	risk assessment). Suitable gloves for
	vapours or suspended matter (e.g.	with the product.	single use are marked with a beaker
	closed systems), the work surface	- Protect spray cans from heating up	according to DIN EN 374.
	shall hazardous gases, vapours or	to more than 50 °C.	- They must be made in such a way
	suspended solids (e.g. closed	- Do not place filled spray cans in a	that they can be worn under normal
	systems), the installation of mixing	shop window.	working conditions,
	and decanting workplaces may be	- Do not direct the spray jet of a spray	e.g. when putting on and taking off
	dispensed with.	can at naked flames or glowing parts.	or when washing out chemicals.
	(3) A special hand-washing and	- Do not spray on people who smoke	- They should also not be sensitising
	hand-care station with a	or smoke while spraying.	to pre-damaged skin.
	temperature-regulated water supply	- Only carry out spraying work in	- They must be of a size and fit to suit
	must be available for employees.	adequately ventilated rooms,	the user's hands. This means that
	This place must be equipped with	depending on the extent of the work.	protective gloves may have to be
	skin protection, skin cleansing and	- Rooms with ventilation are	provided in different sizes.
	skin care products, as well as	considered to be adequately	- The cuffs of washing gloves must
	single-use and towels for single	ventilated provided that only	extend well above the wrist so that
	use.	hairspray of the usual size is used.	

(4) Under the conditions of the	- Do not use aerosol cans if they are	no liquid wrist so that no liquid can
hairdressing trade, health reasons	leaking or have other defects that	enter the inside of the glove.
require the provision of easily	impair the function or safety.	(3) Disposable gloves must be used
accessible break rooms to any	- Safely dispose of empty spray cans.	when working with hairdressing
employee. These must be rooms		chemicals.
enclosed on all sides in which		Disposable gloves must be disposed
hazardous substances may neither		of after one use and must not be
be stored nor used.		reused under any circumstances.
		(4) A skin protection plan must be
		displayed in a clearly visible place in
		every hairdressing salon (e.g. at the
		hand care station). The plan must be
		clearly and easily comprehensible.
		The necessary protective, cleaning
		and care measures must be assigned
		to the various activities in a clear and
		easily understandable form. A
		prerequisite for the acceptance is that
		all company-specific skin-hazardous
		activities that are hazardous to the
		skin, including protective measures.
		(5) The employer shall consult the
		workers concerned on the choice of
		suitable protective equipment and
		the conditions under which it is to be
		used.