Patch testing with hair cosmetic series in Europe: a critical review and recommendation

Wolfgang Uter[1], Lynda Bensefa-Colas[2,3], Peter Frosch[4], Ana Giménez-Arnau[5], Swen M. John[6], Jean-Pierre Lepoittevin[7], Carola Lidén[8], Ian R. White[9] and Jeanne Duus Johansen[10]

[1]*Department of Medical Informatics, Biometry and Epidemiology, Friedrich-Alexander University Erlangen-Nürnberg, D-91054 Erlangen, Germany,* [2]*Occupational Diseases Department, University Hospital of Centre of Paris COCHIN, AP-HP, 75014 Paris, France,* [3]*Laboratoire Santé Publique et Environnement, EA 4064, Paris Descartes University, Sorbonne Paris Cité, 75014 Paris, France,* [4]*Department of Dermatology, University of Witten/Herdecke and Klinikum Dortmund (formerly), 44137 Dortmund, Germany,* [5]*Department of Dermatology, Hospital del Mar, Institut Mar d´Ínvestigacions Mediques Universitat Autònoma, 08003 Barcelona, Spain,* [6]*Department of Dermatology, Environmental Medicine and Health Theory, University of Osnabrueck, 49076 Osnabrueck, Germany,* [7]*Laboratoire de Dermatochimie ILB, CNRS, University of Strasbourg, F-67081 Strasbourg, France,* [8]*Institute of Environmental Medicine, Karolinska Institutet, SE-17177 Stockholm, Sweden,* [9]*St John's Institute of Dermatology, St Thomas' Hospital, London, SE1 7EH, UK, and* [10]*Department of Dermato-Allergology, National Allergy Research Centre, Gentofte Hospital, University of Copenhagen, 2900 Hellerup, Denmark*

doi:10.1111/cod.12424

Summary

Many key ingredients of hair cosmetics (in particular, dyes, bleaches, and hair-styling agents) are potent (strong to extreme) contact allergens. Some heterogeneity is apparent from published results concerning the range of allergens for which patch testing is important. The objective of the present review was to collect information on the current practice of using 'hair cosmetic series', and discuss this against the background of evidence concerning consumer/professional exposure and regulatory aspects to finally derive a recommendation for a 'European hair cosmetic series'. The methods involved (i) a survey targeting all members of the COST action 'StanDerm' (TD1206) consortium, (ii) analysis of data in the database of the European Surveillance System on Contact Allergies (ESSCA), and (iii) literature review. Information from 19 European countries was available, partly from national networks, and partly from one or several departments of dermatology or, occasionally, occupational medicine. Apart from some substances being tested only in single departments, a broad overlap regarding 'important' allergens was evident. Some of the substances are no longer permitted for use in cosmetics (Annex II of the Cosmetics Regulation). An up-to-date 'European hair cosmetics series', as recommended in the present article, should (i) include broadly used and/or potent contact allergens, (ii) eliminate substances of only historical concern, and (iii) be continually updated as new evidence emerges.

Key words: contact allergy; diagnostic patch testing; hair cosmetics; standardization.

Many chemicals used in the various cosmetic treatments of human hair are strong or even extreme contact allergens, and may therefore cause contact allergy and result in allergic contact dermatitis (1). Hence, patients undergoing patch testing for evaluation of dermatitis possibly related to hair cosmetics are routinely tested with an additional patch test series containing a collection of important ('indicator') hair cosmetic ingredients. Guidelines on patch testing have been published (2). Commercial suppliers of patch test materials, except for the TRUE Test®, cater for this need by providing ready-to-order test series termed 'hair cosmetics series' or 'hairdresser series'. Information on suppliers of patch test materials is available from the European Society

Correspondence: Wolfgang Uter, Department of Medical Informatics, Biometry and Epidemiology, Friedrich-Alexander University Erlangen-Nürnberg, Erlangen, Waldstr. 4-6, D-91054 Erlangen, Germany. Tel: +49 9131 8522750; Fax: +49 9131 8522721. E-mail: wolfgang.uter@imbe.med.uni-erlangen.de

Accepted for publication 27 April 2015

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

of Contact Dermatitis (ESCD) website (www.escd.org). Patients who may be tested with such a test series include consumers/self-users of hair cosmetics, clients of hairdressers, and hairdressers themselves. Hairdressers are often patch tested because of suspected allergic contact dermatitis affecting their hands; the diagnostic appropriateness of the series is crucial against the background of the success of secondary prevention (including keeping patients with occupational contact dermatitis at work) and the medico-legal consequences. It has been stressed that patch testing should be undertaken as a matter of policy in all hairdressers with dermatitis, even if primarily irritant and/or atopic dermatitis is suspected (3). However, a closer look at the composition of existing hairdressing series reveals shortcomings: (i) a number of (newly introduced) chemicals are not included, although occasional or even important contact allergens have been found in special studies (4); (ii) conversely, some substances may be included that, for a long period, have been banned from use in hair cosmetics in the EU. The present article reviews current practice regarding the use of hair cosmetics patch test series, and discusses the findings with respect to regulatory requirements and exposure information, to finally derive a conclusion regarding a 'European hair cosmetics series', combined with recommendations on how to proceed if even such an improved series does not provide a conclusive result in terms of 'explaining' the dermatitis that the patient has presented with.

Methods

The first aim of the present study was to collect information on current practice regarding the set of allergens, together with their test concentrations and vehicles, used as 'hair cosmetics series' in dermatological (including occupational dermatology) departments across Europe. For this purpose, several approaches were used:

- Members of the StanDerm consortium (www.standerm.eu), which provides nearly complete geographical coverage of Europe, were requested by e-mail to fill in a simple electronic questionnaire (spreadsheet) listing the allergens used locally.
- Publications in the last 10 years were screened via PubMed, with the search terms 'hairdresser allergy' and 'hair cosmetic allergy', in order to identify reports containing the above information (actual patch test results, and aspects raised in the discussion of these, were also used).
- The database of the European Surveillance System on Contact Allergies (ESSCA) (www.essca-dc.org), containing patch test results since 2002 and information on the patch test series used to obtain these, was searched to identify hair cosmetics series in addition to those provided by ESSCA members responding to the StanDerm survey.

The CosIng database was used to retrieve additional information, including INCI names, function(s), CAS numbers, reference to regulation (Annex II or Annex III of the Cosmetics Regulation EC 1223/2009), including maximum permitted use concentrations in the product, and opinions and statements by the Scientific Committee on Consumer Safety (SCCS) and its predecessors. As of 1 October 2014, CosIng (http://ec.europa.eu/consumers/cosmetics/cosing/, last accessed 14 February 2015) included 211 substances or partly mixtures or salts used for 'hair dyeing', 191 used for 'hair fixing', 59 used for 'hair waving or straightening', 29 used for 'oxidizing', and a large number of substances used for purposes pertinent to, but not specific for, hair cosmetics, such as preservatives and fragrances. CosIng is an indicative but not exhaustive database of cosmetic ingredients maintained by the European Commission.

Concerning the second aim, to provide a recommended European hair cosmetics series, substances that were to be regarded (i) as proven, common contact allergens, or (ii) as more rare allergens, with, however, widespread exposure, would qualify for inclusion in the European hair cosmetics series. Other substances with less evidence concerning importance as contact allergens clinically, but with widespread exposure, which also need further investigation, would be included in a supplemental test series, used predominantly in specialized departments and scientifically evaluated in the short term.

Results

Information was eventually obtained from 19 European countries. There was some information based on recommendations of national contact dermatitis research groups [e.g. the British Society of Cutaneous Allergy (5), the Danish Contact Dermatitis Research Group (6), and the German Contact Dermatitis Research Group (7)], and information from responses or reports from single departments. The set of substances identified with the above combined strategies are shown in Table 1.

The use of substances in current hair cosmetics series is shown in Table 2, by providing information on the number of countries (represented by a network, or by one or several departments) using the respective substance. In addition to the substances shown in Table 2, a number of test preparations were used by single departments in different countries. These are shown in Table S1.

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

Table 1. Substances used in hair cosmetics that have been employed in a 'hair cosmetic series' in at least one department

INCI name	Other names(s)	CAS no.	Function	Annex	Opinion(s) categorization	Maximum concentration (%)
m-Aminophenol	3-Aminophenol (CI 76545)	209-711-2	Hair dyeing	III/217	SCCP/0978/06, SCCNFP/0231/99***	1.2
p-Aminophenol	–	123-30-8	Hair dyeing	III/272	SCCP/0867/05	0.9
Ammonium persulfate	Diammonium peroxodisulfate	7727-54-0	Bleaching, oxidizing	–	–	–
Ammonium thioglycolate	Ammonium mercaptoacetate	5421-46-5	Depilatory, hair waving or straightening, reducing	III/2a	–	8–11
Ammonium thiolactate	Ammonium 2-mercaptopropionate	13419-67-5	Depilatory, hair waving or straightening, reducing	–	–	–
Benzoyl peroxide	Dibenzoyl peroxide	94-36-0	Oxidizing	III/94	–	0.7
Chloroacetamide	2-Chloroacetamide	79-07-2	Preservative	V/41	SCCS/1360/10	0.3
Cocamide DEA	Amides, coco, *N*,*N*-bis(hydroxyethyl)	68603-42-9	Emulsifying, emulsion stabilizing, foam boosting, surfactant, viscosity controlling	III/60	–	[a]
Cocamidopropyl betaine	1-Propanaminium, 3-amino-*N*-(carboxymethyl)-*N*, *N*-dimethyl and *N*-coco acyl derivatives, hydroxides, inner salts	61789-40-0	Antistatic, cleansing, foam boosting, hair conditioning, surfactant, viscosity controlling	–	–	–
Cocamidopropyl dimethylamine	Amides, coco, *N*-[3-(dimethylamino)propyl]	68140-01-2	Antistatic, emulsifying, hair conditioning, surfactant	–	–	–
Cysteamine HCl	Mercaptamine hydrochloride	156-57-0 (as HCl)	Antioxidant, hair waving or straightening, reducing	–	–	–
Decyl glucoside	Decyl D-glucoside	54549-25-6	Cleansing, surfactant, emulsion stabilizing	–	–	–
Ethanolamine	Monoethanolamine	141-43-5	Buffering	III/61	–	[a]
Glyceryl thioglycolate	Mercaptoacetic acid, monoester with propane 1,2,3-triol	30618-84-9	Hair waving or straightening	III/2b	–	8–11
Hydrogen peroxide	–	7722-84-1	Antimicrobial, oxidizing	III/12	–	12
4-Hydroxypropylamino-3-nitrophenol	1-Hydroxy-3-nitro-4-(3-hydroxypropylamino) benzene	92952-81-3	Hair dyeing	III/205	NC	2.6
Lauryl glucoside	D-Glucose homopolymer, dodecyl ether	110615-47-9	Cleansing, surfactant	–	–	–
p-Methylaminophenol	4-Methylaminophenol	150-75-4	Hair dyeing	III/223	SCCNFP0179/99, SCCP/0963/05**	0.68[b]
1-Naphthol	1- Naphthalenol	90-15-3	Hair dyeing	III/16	SCCNFP/0130/99, SCCP/1123/07***	1
Oleamidopropyl dimethylamine	–	109-28-4	Antistatic	–	–	–

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

Table 1. Continued

INCI name	Other names(s)	CAS no.	Function	Annex	Opinion(s) categorization	Maximum concentration (%)
p-Phenylenediamine	Benzene-1,4-diamine (CI 76060)	106-50-3	Hair dyeing	III/8a	SCCNFP/0129/99, SCCP/0989/06****	–
p-Phenylenediamine; *p*-phenylenediamine HCl; *p*-phenylenediamine sulfate	*p*-Phenylenediamine and its salts	106-50-3/624-18-0/16245-77-5	Hair dyeing	III/8b	****	2
N-phenyl-*p*-phenylenediamine sulfate	bis(*N*-Phenylbenzene-*p*-diamine) sulfate (CI 76085)	4698-29-7	Hair dyeing	III/8	SCCP/0991/06****	3
Potassium persulfate	Dipotassium peroxodisulfate	7727-21-1	Oxidizing	–	–	–
Resorcinol	(CI 76505)	108-46-3	Hair dyeing	III/22	SCCP/1117/07, SCCS/1270/09***	2.5
Thioglycolic acid	Mercaptoacetic acid	68-11-01	Antioxidant, depilatory, hair waving or straightening, reducing	III/2a	SCCS 1520/13	8–11
Thiolactic acid	2-Mercaptopropionic acid	79-42-5	Antioxidant, depilatory, hair waving or straightening, masking, reducing	–	–	–
Toluene-2,5-diamine	2-Methyl-*p*-phenylenediamine (CI 76042)	95-70-5	Hair dyeing	III/9a	SCCP/1084/07, SCCS/1479/12****	4
Toluene-2,5-diamine sulfate	–	615-50-9	Hair dyeing	III/9a	SCCS/1479/12****	4
Triethanolamine	Trolamine	102-71-6	Buffering, emulsifying, masking, surfactant	III/62	–	2.5[a]
Zinc pyrithione	Pyridine-2-thiol-1-oxide, zinc complex (2:1)	13463-41-7	Antidandruff, antiseborrhoeic, hair conditioning, preservative	III/101; V/8	SCCS/1512/13	0.1

INCI name (if none exists, the common name is given in parentheses), chemical name (if different/existing), function according to CosIng (if none exists, the substance is not included in this inventory), CAS number, regulatory information, and use restrictions. Substances not permitted in cosmetics (Annex II of Cosmetics Regulation) are not listed, but are mentioned in the text. Maximum concentration: maximum permitted concentration in the product after mixing, calculated as free base/acid.
SCCS categorization of hair dye sensitizing potency according to guideline tests (1) (free base and salts treated the same): ****extreme; ***strong; **moderate; NC, non-classifiable.
[a]Maximum secondary amine content: 0.5%.
[b]Calculated as sulfate.

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

Table 2. Actual use of hair cosmetic substances in hair cosmetic series in networks (Information Network of Departments of Dermatology, representing three countries: Austria, Germany, and Switzerland)

INCI name	%	Vehicle	n (networks)	n (departments)	Remarks
4-Aminoazobenzene[a] (CAS no. 60-09-3)	0.25	pet.	–	3	In one department: 1%
m-Aminophenol	1	pet.	5	13	–
p-Aminophenol	1	pet.	5	13	–
Ammonium persulfate	2.5	pet.	4	15	Partly also 1% pet. and 2.5% aq.
Ammonium thioglycolate	2.5	aq.	5	14	Partly also 1% aq.; a few use 2% pet.
Ammonium thiolactate	2.5	pet./aq.	–	2	–
Captan[a] (CAS no. 133-06-2)	0.5	pet.	1	7	–
Chloroacetamide	0.2	pet.	1	7	–
Cocamide DEA	0.5	pet.	–	2	–
Cocamidopropyl betaine	1	aq.	4	10	–
Decyl glucoside	3; 5	pet.	–	2	–
3-Dimethylaminopropylamine	1	aq.	–	5	One department stated 'pet.'
Disperse Orange 3[a] (CAS no. 730-40-5)	1	pet.	–	2	–
Ethanolamine (monoethanolamine)	2	pet.	3	1	–
Glyceryl thioglycolate	1	pet.	5	14	–
Hydrogen peroxide	3	aq.	1	9	–
Hydroquinone[a] (CAS no. 123-31-9)	1	pet.	4	10	–
Lauryl glucoside	3	pet.	–	2	–
1-Naphthol	1	pet.	–	2	–
2-Nitro-*p*-phenylenediamine[a] (CAS no. 5307-14-2)	1	pet.	2	13	–
Oleamidopropyl dimethylamine	0.1	aq.	–	7	–
p-Phenylenediamine	1	pet.	5	14	Part of the European baseline series
Pyrocatechol[a] (CAS no. 120-80-9)	2	pet.	–	2	–
Pyrogallol[a] (CAS no. 87-66-1)	1	pet.	3	8	–
Resorcinol	1	pet.	2	15	Tested at 2% in four departments
Toluene-2,5-diamine	1	pet.	4	5	–
Toluene-2,5-diamine sulfate	1	pet.	1	13	Very rarely in parallel with free base; differences between departments in one country
Zinc pyrithione	1	pet.	1	7	–

n(networks): number of countries represented by networks. n(departments): number of countries represented by one or more departments. CAS no. additionally given for substances not listed in Table 1.
[a]Use currently not permitted in cosmetics.

Discussion

A discussion of the composition of a basic European hair cosmetics series considered to be optimal at the time of writing is given below, and summarised in Table 3, with possible extensions being shown in Table 4. It should be noted that this hair cosmetics series does not, with a few exceptions, include preservatives, and it does not include fragrances or ultraviolet (UV) filters, although these are common ingredients, and well-known allergens, in these cosmetic product categories (8–10). Hence, more extended patch testing with preservatives, fragrances, or other substances beyond the markers included in the baseline series, which should normally always be applied, should be considered, on the basis of the patient's history. Before different types of hair cosmetic ingredients are discussed in a strict sense, the need to continually adapt such a series, thus maintaining a high degree of diagnostic relevance, will be generally discussed.

General considerations for including substances in a test series

The basis of keeping a European hair cosmetics series useful is its continual re-evaluation based on clinical (contact allergy) and exposure data, which may depend on changes in regulation, fashion, and development. Concerning clinical data, case reports often provide the first hints that a substance is an allergen. Cosmetovigilance systems in terms of dermatological networks are able to collect several case reports, or perform *ad hoc* investigations into new putative allergens within the network. However, only clinical studies evaluating new allergens in a sufficiently large number of patients will also provide solid data concerning the suitability of the chosen patch test concentration and vehicle (e.g. 4).

The selection of substances for assessment in such studies may be guided by case reports and cosmetovigilance results, but also by considering the amount of

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

Table 3. Suggested core European hair cosmetic series; all allergens are available as commercial patch test preparations

INCI name	CAS no.	% (vehicle)	Comment
m-Aminophenol	209-711-2	1.0 (pet.)	–
p-Aminophenol	123-30-8	1.0 (pet.)	–
Ammonium persulfate	7727-54-0	2.5 (pet.)	–
Ammonium thioglycolate	5421-46-5	1 to 2.5 (aq.)	Patch test material freshly prepared from stock solution is preferable
Glyceryl thioglycolate	30618-84-9	1.0 (pet.)	–
p-Methylaminophenol sulfate	150-75-4	1.0 (pet.)	Available as photographic developer Metol®, CAS no. 55-55-0, until the free base is commercially available for patch testing
p-Phenylenediamine	106-50-3	1.0 (pet.)[a]	If not in baseline series already (at this concentration)
Resorcinol	108-46-3	1.0 or 2.0 (pet.)	–
Toluene-2,5-diamine	95-70-5	1.0 (pet.)	The sulfate is a less sensitive diagnostic tool

[a]In patients with a history of reactions to 'henna tattoos', the initial patch test concentration should be lower by 1 or 2 orders of magnitude, or patch test exposure time should be reduced to one to a few hours (11), to avoid unnecessarily strong patch test reactions.

Table 4. Allergens suggested as temporary additions to a European hair cosmetic series for monitoring purposes; allergens are available as commercial patch test preparations, except where indicated otherwise

INCI name	CAS no.	% (vehicle)	Reference
4-Amino-2-hydroxytoluene	2835-95-2	[a]	–
Chloracetamide	79-07-2	0.2 (pet.)	(6)
Cocamide DEA (coconut diethanolamide)	68603-42-9	0.5 (pet.)	–
Cocamidopropyl betaine	61789-40-0	1 (aq.)	–
Cysteamine HCl	156-57-0	0.5 or 1 (pet.)	(6, 12, 13)
Decyl glucoside	54549-25-6	5 (pet.)	(14)
Hydroxyethyl-*p*-phenylenediamine sulfate	93841-25-9	1 or 2 (pet.)	(15)
Lauryl glucoside	110615-47-9	3 (pet.)	(14)
2-Methylresorcinol	608-25-3	[a]	–

[a]A pragmatic approach would be to test 1% pet.; the national legal framework must be considered when non-licensed materials are tested.

exposure of the (occupational or consumer) population together with the presumptive risk associated with the substance (potency and use concentration). Different surveys of cosmetic ingredient labelling of permanent (oxidative) hair dyes have provided valuable insights into the frequency of use in different markets (16–18) (S Kirchlechner, pers. comm. 2014). Søsted et al. systematically compiled the available information in 2004, and provided a ranking concerning contact allergy risk, which can serve to prioritize assessment in clinical studies (19). The SCCS and its predecessor compiled animal data on the skin-sensitizing potency of hair dye substances. It was shown that ~50% of 114 assessed hair dye substances are skin sensitizers, and that at least 36 of them are strong or extreme sensitizers (1, 20).

Concerning substances that are currently not permitted for use in hair cosmetics (e.g. those included in Annex II to the Cosmetics Regulation), inclusion in a European hair cosmetics series seems to be unnecessary. However, for a certain period after banning, it may be important to keep such substances on the test series, to enable the diagnosis of 'historical' contact allergy, especially in a medico-legal context. Two 'coupling agents' for oxidative hair dyes commonly found in hair cosmetics series (Table 2) are pyrogallol and hydroquinone. Both were banned from use in hair dyes as early as 1994 (Annex II/409 and Annex II/1339, respectively; CosIng database). Similarly, the less often used pyrocatechol was delisted in 1994 (Annex II/408; CosIng database). Therefore, these substances should probably not be included in a European hair cosmetics series. Surprisingly, notable proportions of patients sensitized to hydroquinone and pyrogallol have been identified even in more recent years (5, 7). In the latter study, sensitized patients were identified in whom relevant exposures would be considered to be unlikely, in view of their age. Hydroquinone is permitted in artificial nail systems in use concentrations up to 0.02% after mixing (Annex III/14), and illegal skin-bleaching products imported into the EU may be a source of exposure (as well as prescribed medical products), including bleaching products containing the derivative arbutin (CAS no. 497-76-7); sensitization to arbutin has hitherto been reported only from Japan (21). Hydroquinone may also be present in a few chemical products to which there is occupational exposure. Despite the above, chemical cross-reactivity via the oxidation product *p*-quinone (1,4-benzoquinone) must be considered as the explanation for the observed positive patch test reactions.

Hair dyes

Hair-dyeing products can be subdivided into oxidative and non-oxidative ('temporary', 'shading', etc.) colourings. Use of a product of the first type usually involves

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

the application of mostly colourless dye monomers, which enter the hair shaft, become polymerized *in situ* by an oxidizing agent, and thus, as a molecule, become (i) coloured and (ii) too big to leave the hair shaft again, thus achieving a colouration effect lasting for many weeks (notwithstanding some decay resulting from UV light and other factors). The molecules involved are both small and chemically reactive, which makes them ideal haptens. Indeed, the common components of oxidative hair dye products, which are sometimes subdivided into basic substances and couplers from a technical point of view, have been shown to be mostly strong or even extreme sensitizers (1, 20).

Among the 'basic substances', *p*-phenylenediamine (PPD), toluene-2,5-diamine [TDA; synonym *p*-toluene diamine (PTD)] and *p*-aminophenol have a well-proven record of frequently eliciting positive patch test reactions (e.g. 6, 7, 22). Hence, their inclusion in a European hair cosmetics series, or, in the case of PPD, even in the baseline series, owing to the overall significance in other exposure areas (23, 24), is well justified. PTD and *p*-aminophenol are frequently found ingredients of oxidative hair dyes, according to market surveys from Sweden (11), Denmark (20), Spain (12), and Germany (S Kirchlechner, pers. comm. 2014), but may also be found in direct hair dyes. In contrast, the use prevalence of PPD apparently varies, and has been found to be low in the Swedish (16) and Danish (25) markets, and very low in the current German market (S Kirchlechner, pers. comm. 2014).

In the context of patch testing, the question of multiple contact allergy is important – in this case, with a view to potentially eliminating the need for testing long sets of allergens that, when truly cross-reactive, may give rise to many unnecessary, possibly strong or extreme, patch test reactions. However, if cross-reactivity is suggested on the basis of clinical data, the possibility that previous exposure to chemically related substances, with independent sensitization, has occurred cannot usually be excluded. Thereby, cross-reactivity in the original sense (26) will be overestimated. Clinical data suggest that using PPD alone as a screening agent is not adequate, as it will fail to diagnose an important proportion of patients sensitized to PTD (TDA), *p*-methylaminophenol (4), and other components (27). Substances with proven, direct transformation to common haptens, such as PPD, Disperse Orange 3, and *p*-aminoazobenzene, may be exceptions. Otherwise, only in the negative case of a lack of concomitant reactivity can cross-reactivity be excluded, on the assumption, of course, that appropriate patch test conditions (concentration, vehicle, exposure time, and reading) have been used (2). Cross-reactivity based on clinical data can only be validly assessed if a new substance, to which previous exposure can be excluded, is, for instance, patch tested in persons sensitized to the main allergens PPD or PTD. This has been performed for the basic substance hydroxyethyl-*p*-phenylenediamine sulfate, a 'modified PPD', and it was found that the majority of, but not all, study participants sensitized to PPD or PTD tolerated a patch test with the new agent, tested at 1% and 2% pet. (15). However, this result does not preclude the possibility that hydroxyethyl-*p*-phenylenediamine sulfate is a sensitizer in its own right, and will cause contact allergy independently following marketing [the share of products with this agents was already higher than the share of products with PPD in Germany in October 2014 (S Kirchlechner, pers. comm. 2014)]. Therefore, hydroxyethyl-*p*-phenylenediamine sulfate is a candidate for close surveillance.

Under the alkaline conditions in the mixed hair dye product, PTD and PTD sulfate can be considered to be equivalent (A Schuh, pers. comm. 2014). However, both PTD free base and PTD sulfate are used as patch test preparations, and this may make a relevant difference. First, with 1% as the test concentration, the concentration of PPD base is (nominally, see below) 1%, but with the sulfate, it is 0.56%. However, the nominal test concentration of the free base declines rapidly, for example to 0.2% within 2 months (28). However, the diagnostic quality does not decline, which led the authors to speculate that not (only) the monomer, but also oligomers and possibly degradation products, act as haptens (28). Allegedly, the sulfate is more stable as a patch test preparation, but it has been shown to detect substantially fewer cases of sensitization than the free base [7.4% versus 14.3% of 191 patients (29) and 8.4% versus 18.0% of 178 patients (30), respectively], and is therefore not as recommendable for patch testing.

Regarding so-called coupling agents used to determine the shade of the colouring, a variety are used (S Kirchlechner, pers. comm. 2014). Only some are represented in the hair cosmetics series series (Table 2). *m*-Aminophenol is among the most frequently used, is a well-recognized contact allergen (6, 5), and is thus a legitimate component of any hair cosmetics series. Resorcinol is used in > 80% of oxidative hair dye products (16–18), but is probably a comparatively rare sensitizer, with sensitization frequencies as low as 1 of 191 (25), 1 of 283 (6), 3 of 2939 (4) or 2 of 501 (5) relevant positive reactions. As compared with other ingredients, considering the widespread use and low sensitization frequency, resorcinol is considered to be a weak sensitizer. Resorcinol is, however, a strong sensitizer, with an EC3 value of 1.4% according to the local lymph node assay in mice (31). Some departments test resorcinol at 2%

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

and not at the mostly used 1%; however, comparative studies addressing the optimal patch test concentration are lacking. 2-Nitro-*p*-phenylenediamine is a moderately common hair dye allergen, with 11 of 189 (25), 3 of 281 (6) and 37 of 428 (5) positive reactions, and was used in semi-permanent hair dyes (5). In June 2008, the substance was delisted (II/1319; CosIng database). Hence, even if a few years are allowed for diagnosing 'historical sensitization', it does not appear to be necessary to include this substance any longer. 1-Naphthol has been found in a small number of professional products on the German market (S Kirchlechner, pers. comm. 2014). In the European multicentre study, no positive reactions in 736 patients have been observed (4). Hence, inclusion in at least a base hair cosmetics series (Table 3) does not seem to be warranted. 4-Aminoazobenzene (*p*-aminoazobenzene) is banned from use in cosmetics (Annex II/990; CosIng database), as is Disperse Orange 3 (Annex II/1281), and thus neither needs to be included in a hair cosmetics series. Furthermore, cross-reactivity between Disperse Orange 3 and PPD has been found to be so marked in the past that PPD would suffice as a screening marker (32).

A European multicentre study (4) observed that '*p*-Methylaminophenol gave a reaction in 20 patients (2.2%), 3 of them with clinical relevance, and no co-reaction with five well-known hair dyes'. Hence, the regular inclusion of this ingredient would appear to be worthwhile, also to gather further data on the frequency of contact allergy, despite it being commercially available only as the sulfate (Table 3). The same holds true for a modified PPD that has been found to only very partially cross-react with PPD in sensitized patients (15), but that needs to be kept under surveillance concerning its inherent sensitizing risk, namely, hydroxyethyl-*p*-phenylenediamine sulfate. We suggest the inclusion of this substance in the extension part of the series (Table 4). 2-Methylresorcinol and 4-amino-2-hydroxytoluene are two of the most frequently used hair dye substances in Germany (S Kirchlechner, pers. comm. 2014), Spain (12), Sweden (11, and the United States (13), occurring in ~35% of oxidative hair dye products. On the basis of this, we suggest that both substances should be included in the extension part of the series (Table 4). Pragmatically, a patch test concentration of 1% pet. could be used, although this should be verified.

Henna is a vegetable dye derived from the henna plant (*Lawsonia inermis*). It is widely used in countries such as India and Tunisia for colouring hair, hands, or fingernails. The active ingredient is lawsone (2-hydroxy-1,4 naphthoquinone; CAS no. 83-72-7). Although 'henna tattoos' have become known as materials causing severe contact allergic reactions, the actual cause of these is adulteration with sometimes extreme concentrations of PPD (33) and subsequent severe sensitization to PPD. However, there are few case reports of proven contact allergy to henna itself, tested as a paste made from the leaves (pure or 10% pet.) in lieu of a commercially available test preparation (34, 35), or to lawsone, as far as this has been tested (36). In 2013, the SCCS concluded that (with large clinical studies lacking) 'there are rare case reports of contact allergy to Henna in the literature and rare immediate hypersensitivity reactions' (SCCS/1511/13); the latter must be considered in users of henna powder suffering from asthma, rhinitis or contact urticaria (37, 38).

Bleaching agents

Ammonium persulfate is included in most hair cosmetics series, and, considering the frequency of contact allergies (5–7, 22), this is very well justified, in the context of patch testing of both hairdressers and clients/consumers. It is unclear whether additional testing with other persulfate salts, for example potassium persulfate, will detect additional relevant cases of contact sensitization (in the case of prick testing for immediate-type hypersensitivity, this has been observed; see below).

Hydrogen peroxide is a component of many agents used for the treatment of hair, including oxidative hair dyes, but also bleaches and permanent-wave agents. It is tested at 3% aq., and is included in the hair cosmetics series of one Swedish provider. However, allergic reactions seem to be exceedingly rare, and have, in fact, not been observed in several reported series in which several hundred patients were tested (5, 39). Hence, there is no point in patch testing with hydrogen peroxide.

Although the present article addresses patch testing for suspected contact allergy, it must be mentioned that, occasionally, immediate-type hypersensitivity (clinically manifesting as rhinitis, bronchial asthma, and contact urticaria) to hair-bleaching products is observed in hairdressers and in their clients. The most common allergens are ammonium persulfate and potassium persulfate, which apparently do not necessarily cross-react (40) and should normally be tested freshly prepared in water, not in pet., as in the patch test. In cases of strong, immediate-type sensitization, patch testing with the respective allergen may entail a certain risk of generalized anaphylactic reactions.

Waving and straightening agents

Glyceryl thioglycolate [also: glyceryl monothioglycolate (GMTG)] is a constituent of 'acid perming solutions'.

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

Some years after its introduction onto the German marked, an epidemic of contact allergy in hairdressers was observed (29); clients have also been found to be sensitized, although not as frequently. A similarly high prevalence was observed in a Dutch specialized clinic, in terms of 59 of 103 hairdressers identified as being contact allergic (41). In the mid-1990s, GMTG was voluntarily withdrawn from the German market by the main producers, and this was followed by a ban on the professional use of GMTG by hairdressers in the 'Technical Rules for Hazardous Substances 540'. Within a few years, the success of this intervention was confirmed by a massive reduction in the prevalence of sensitization in patch tested hairdressers, reaching 0% in the youngest age group, who were presumably not exposed after the ban (42). However, recently, some re-emergence of GMTG sensitization in Germany has been noted (7), which further points to the need to keep a cosmetic allergen in the patch test series for some time after exposure should have ceased. Interestingly, the prevalence rates of sensitization in other countries were never reported to be as high, for example 8.4% in the United Kingdom (albeit probably not only in hairdressers, but also in clients) (5) or just 1.0% in a recent Danish study (6). Such variations in the prevalence rates of sensitization most likely reflect geographical differences in usage and, possibly, also the effectiveness of skin protection. Nevertheless, it seems warranted to include GMTG in a European hair cosmetics series.

In contrast to GMTG, ammonium thioglycolate has been used widely for many decades, without a record of being a frequent contact sensitizer, with, for example, 1 of 371 patients being found to be contact-allergic in (6), 4 of 504 in the United Kingdom (5), and 9 of 702 among hairdressers and 6 of 1676 among clients in the most recent Information Network of Departments of Dermatology (IVDK) data (7). Concerning the test concentration and vehicle used, some variation in current practice exists. After a previously marketed test preparation at 1% pet. had proven unstable, according to investigations by Hermal, Reinbek, Germany ('Kontaktallergie aktuell', April 2002), freshly prepared allergen was recommended. Currently, freshly prepared ammonium thioglycolate 1% aq. is recommended by the German Contact Dermatitis Research group. One commercial producer offers 2.5% ammonium thioglycolate in water; the stability of this preparation has not been assessed (B Niklasson, pers. comm. 2014).

The role of ammonium thiolactate and thiolactic acid, which are contained in so-called 'ester-free' permanent-wave solutions, has been evaluated in a study by the German Contact Dermatitis Research group. Ammonium thiolactate 1% pet. was found to be chemically unstable, as was thiolactic acid at concentrations of $< 0.1\%$ in pet. Ammonium thiolactate 2% aq. caused weak positive reactions in 7 of 177 patients tested, and ammonium thiolactate 1% aq. in 4 of 291 patients tested. Additionally, a positive result in a repeated open application test with ammonium thiolactate 1% aq. was observed in 1 of the 3 patients who were patch test-positive for ammonium thiolactate or thiolactic acid assessed with this method. Thiolactic acid at 1% pet. was highly irritating; after application of thiolactic acid 0.3% pet., infiltrated and erythematous reactions were observed in 5 of 393 patients tested; however, questionable or irritant reactions were observed in 42 of 393 (10.7%) patients. In conclusion, ammonium thiolactate should be regarded as a potential allergen, whereas thiolactic acid, which is included in product concentrates up to a concentration of 1% only, appears to be basically an irritant (43).

Cysteamine HCl, which is included typically at concentrations between 5% and 12% [after (12)], has been identified as an 'emerging allergen' in a recent study (6), albeit based on just one positive reaction in 12 hairdressers tested. A previous report has described one case and a clinical series, in which (in The Netherlands), among 1347 hairdressers patch tested in 1994–2004 with 0.5% cysteamine HCl, 16 positive patch test reactions, all assessed as being of current clinical relevance, were found (12). Even earlier, a case of contact sensitization to cysteamine HCl in a hairdresser was described in the United States; patch testing with 1% pet. gave negative results in 64 controls (13). Thus, this permanent-wave agent should probably be included in a hair cosmetics series, at least temporarily for monitoring purposes, to provide further evidence on its role as a sensitizer.

Antimicrobial substances and preservatives

A preservative is used in a cosmetic product primarily to inhibit the growth of microorganisms in the product; allowed preservatives are listed in Annex V of the Cosmetics Regulation ('positive list', currently 172 entries). The function of an antimicrobial substance is to help control the growth of microorganisms on the skin (currently, 577 substances in CosIng). There is considerable inconsistency and overlap between the categories. For instance, benzisothiazolinone is listed as an antimicrobial, but is not allowed as a preservative. Preservatives in hair cosmetics are well known to cause allergic contact dermatitis. Only those few included in hair cosmetics series will be addressed below. It is also important to test hairdressers (and probably clients and self-users of hair

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

cosmetics series) not only with the baseline series containing the most important preservatives, but also with additional cosmetic preservatives which are used also beyond hair cosmetics series. This recommendation is motivated by the observation of a relatively high proportion of hairdressers being sensitized to preservatives, which points to inappropriate exposures, probably via rinse-off products, which cumulatively expose hairdressers' hands to sensitizing biocide levels (7, 22).

Several hair cosmetics series include captan (CAS no. 133-06-2), an antimicrobial substance. However, as its use has been prohibited in cosmetics since 1990 (Annex II/370; owing to carcinogenicity), its inclusion in a hair cosmetics series should be reconsidered. Chloroacetamide is permitted as a preservative at concentrations up to 0.3% (Table 1). In the Danish study, 5 of 302 patients were found to be sensitized (6); in a UK study, 2 of 517 patients were found to be sensitized (5); and in France, a case of sensitization attributable to a preserved oxidation product was found (44). Also when consecutive patients were patch tested with chloroacetamide, similar prevalences of contact allergy were noted, for example as many as 2.1% positive reactions, one-third of which were considered to be relevant (past or present; not stated), in 4451 Australian patients (45), or 0.8% positive reactions in 80 824 patients tested with a special series, 'topical antiseptics', in the IVDK (46). According to a market survey of cosmetics conducted in 2006–2009 in Germany, chloroacetamide was hardly used in cosmetics at the time (0.1% of 4680 products) (8). However, because of massive reconsideration of the use of preservatives, this may have changed in the meantime, or may change in the future, albeit most likely not only affecting hair cosmetics, but also other rinse-off and leave-on cosmetics. As this is true for almost all preservatives [the authors are not aware of a preservative that is (almost) exclusively used in hair cosmetics], which are potentially relevant for a much broader range of patients, we generally suggest the inclusion of preservatives in a separate 'cosmetic preservative' or similar series to be tested alongside the hair cosmetics series. Thereby, the hair cosmetics series should include only (mostly) specific antimicrobial substances. One example of a more specific substance is zinc pyrithione (zinc omadine), which is (in the context of cosmetics) exclusively found in shampoo (8), and could thus reasonably be tested in a hair cosmetics series. However, it is apparently a rare allergen, according to the literature, with 0 of 409 (5) and 0 of 286 (6) reactions in recent studies, and a last case report published in 2005 (47). Thus, it may not be necessary to patch test with this compound on a regular basis, but only when there is a history suggestive of eczema caused by an 'anti dandruff' shampoo containing zinc pyrithione.

Auxiliary substances

Cocamidopropyl betaine (CAPB) has been found to be a relatively frequent and apparently often relevant allergen in the past (48). Extensive investigations have identified a number of putative impurities resulting from the production process as causing 'CAPB contact allergy', predominantly 3-dimethylaminopropylamine (49), but also oleamidopropyl dimethylamine and cocamidopropyl dimethylamine (50); the last two substances are used in their own right as an antistatic agent and an emulsifying agent, respectively (Table 1). However, with the purity that is currently achieved, it has been stated that CAPB is a very weak allergen, if it is an allergen at all (51). Nevertheless, during 2002–2009, 15 of 1092 patients patch tested showed allergic reactions to CAPB, and mostly also to its potential impurities mentioned above; 10 cases were considered to be occupationally relevant (50). Concerning occupational exposure, it must be considered that hairdressers, if not wearing suitable gloves, are exposed to hair cosmetics series ingredients at an altogether higher level than consumers, as discussed in the context of preservatives. Coconut diethanolamide is rarely included in hair cosmetics series across Europe (Table 2). A recent analysis of data from the Finnish Institute of Occupational Health showed that none of the 19 occupation-related cases of sensitization was attributable to hair cosmetics (but mainly to metal-working fluids) (52). Cases caused by shampoo or other cosmetic exposure are scarce (53–55). Hence, it may not be necessary to regularly include this allergen in a hair cosmetics series, but it may be interesting for special research interests, and to further elucidate its role as a contact sensitizer. Lauryl glucoside and decyl glucoside are alkyl glucosides, and are widely used in shampoos and various other cosmetics, including some leave-on products (14). During a period of 19 years, 30 patients were identified in Belgium with positive patch test reactions to one or more alkyl glucosides, and these were relevant in terms of shampoo exposure in 12 cases. The authors concluded that contact allergy may be more common than expected (14). Hence, it is suggested that these substances should be included at least in an extended hair cosmetics series to collect further information on their importance as allergens.

Monoethanolamine (MEA) is not infrequently found in hair cosmetics, where it is used as a buffer. Because of this observation, MEA was added to the German hairdresser series, and 13 of 711 hairdressers and 19 of 1694 clients/consumers patch tested in 2007–2012 were found to be positive (7); these prevalences are similar to the previously observed prevalences of 1.8% and 1.9%, respectively (22). This corresponds to the overall observed

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

prevalence of MEA sensitization (56) (whereas, in metal workers with contact with water-based fluids, MEA is an important occupational contact allergen). Similarly, triethanolamine has not been found to be an important hair cosmetics series allergen, beyond an occasional case report (57). Hence, it does not appear to be mandatory to include these substances in a hair cosmetics series.

Hydrolysed wheat protein has been identified as cause of – sometimes severe – immediate, IgE-mediated reactions to liquid soaps, shampoo etc. containing it, particularly if the molecular weight (MW) is relatively high (58). The SCCS concluded that the overall risk is apparently low, and recommended the use of derivatives with a maximum MW of 3500 (59). The dermatologist should be aware of this trigger of immediate hypersensitivity in cases with a suggestive history. The ingredient is not commercially available, but must be obtained from the manufacturer for break-down prick (and possibly patch) testing.

Conclusions

A two-part European hair cosmetics series is suggested, with one set of allergens of proven importance for routine testing of all patients with suspected contact allergy to hair cosmetics, and another set including substances with hitherto less well-proven importance. The latter list should be tested in departments specialized in occupational dermatology, and the results should be scientifically evaluated to decide on inclusion in the first, routine part of a European hair cosmetics series. In individual cases, patch testing with hair cosmetic products, and, in the case of a positive reaction or a suggestive history, with adequately diluted single constituents ('break-down test') is recommended. The results should ideally be collected within a cosmetovigilance network (60).

Acknowledgements

The following colleagues, in addition to the authors, contributed information on the composition of patch test series in their departments or national networks and/or discussion at the 'StanDerm' working group 4 ('Surveillance, risk assessment and allergens') workshop in Trieste, 24 February 2015: Annick Barbaud (Nancy, Fance), Lieve Constandt (Brussels FOD, Belgium), Marie-Noelle Crepy (Paris, France), Razvigor Darlenski (Sofia, Bulgaria), Aleksandra Dugonik (Maribor, Slovenia), Malin Engfeld (Malmö, Sweden), Karel Ettler (Prague, Czech Republic), Rosella Gallo (Genova, Italy), Ana Giménez-Arnau (Barcelona, Spain), Margarida Gonçalo (Coimbra, Portugal), Valeria Kohanka (Budapest, Hungary), Beata Kręczisz and Dorota Chomiczewska-Skora (Lodz, Poland), Francesca Larese Filon (Trieste, Italy), Jelena Macan and Suzana Ljubojevic Hadzavdic (Zagreb, Croatia), Vera Mahler (Erlangen, Germany), Maria Pesonen (Helsinki, Finland), Marie-Louise Schuttelaar (Groningen, The Netherlands), Jan Øivind Holm (Oslo, Norway), Slavomír Urbanček (Banská Bystrica, Slovakia), Marko Vok (Izola, Slovenia), and Mark Wilkinson (Leeds, United Kingdom).

This study was supported by the Horizon 2020 COST action TD 1206 'StanDerm'.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Substances employed in hair cosmetic series in single departments. All allergens in pet., except where indicated otherwise.

References

1 SCCS (Scientific Committee on Consumer Safety). Memorandum on hair dye chemical sensitisation, 26 February 2013, 2013. Scientific Committee on Consumer Safety.

2 Johansen J D, Aalto-Korte K, Agner T et al. European Society of Contact Dermatitis guideline for diagnostic patch testing – recommendations on best practice. *Contact Dermatitis* 2015 (accepted).

3 O'Connell R L, White I R, McFadden J P, White J M L. Hairdressers with dermatitis should always be patch tested regardless of atopy status. *Contact Dermatitis* 2010: **62**: 177–181.

4 Søsted H, Rustemeyer T, Gonçalo M et al. Contact allergy to common ingredients in hair dyes. *Contact Dermatitis* 2013: **69**: 32–39.

5 Katugampola R P, Statham B N, English J S C et al. A multicentre review of the hairdressing allergens tested in the UK. *Contact Dermatitis* 2005: **53**: 130–132.

6 Schwensen J F, Johansen J D, Veien N K et al. Occupational contact dermatitis in hairdressers: an analysis of patch test data from the Danish Contact Dermatitis Group, 2002–2011. *Contact Dermatitis* 2014: **70**: 233–237.

7 Uter W, Gefeller O, John S M, Schnuch A, Geier J. Contact allergy to ingredients of hair cosmetics – a comparison of female hairdressers and clients based on IVDK 2007–2012 data. *Contact Dermatitis* 2014: **71**: 13–20.

8 Uter W, Yazar K, Kratz E-M, Mildau G, Lidén C. Coupled exposure to ingredients of cosmetic products: II. Preservatives. *Contact Dermatitis* 2014: **70**: 219–226.

9 Uter W, Yazar K, Kratz E-M, Mildau G, Lidén C. Coupled exposure to ingredients of cosmetic products: I. Fragrances. *Contact Dermatitis* 2013: **69**: 335–341.

10 Uter W, Gonçalo M, Yazar K, Kratz E-M, Mildau G, Lidén C. Coupled exposure to ingredients of cosmetic products: III.

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

Ultraviolet filters. *Contact Dermatitis* 2014: **71**: 162–169.
11 Ho S G Y, White I R, Rycroft R J G, McFadden J P. A new approach to patch testing patients with para-phenylenediamine allergy secondary to temporary black henna tattoos. *Contact Dermatitis* 2004: **51**: 213–214.
12 Isaksson M, van der Walle H. Occupational contact allergy to cysteamine hydrochloride in permanent-wave solutions. *Contact Dermatitis* 2007: **56**: 295–296.
13 Landers M C, Law S, Storrs F J. Permanent-wave dermatitis: contact allergy to cysteamine hydrochloride. *Am J Contact Dermat* 2003: **14**: 157–160.
14 Gijbels D, Timmermans A, Serrano P, Verreycken E, Goossens A. Allergic contact dermatitis caused by alkyl glucosides. *Contact Dermatitis* 2014: **70**: 175–182.
15 Frosch P J, Kügler K, Geier J. Patch testing with hydroxyethyl-*p*-phenylenediamine sulfate – cross-reactivity with *p*-phenylenediamine. *Contact Dermatitis* 2011: **65**: 96–100.
16 Yazar K, Boman A, Lidén C. Potent skin sensitizers in oxidative hair dye products on the Swedish market. *Contact Dermatitis* 2009: **61**: 269–275.
17 Yazar K, Boman A, Lidén C. *p*-Phenylenediamine and other hair dye sensitizers in Spain. *Contact Dermatitis* 2012: **66**: 27–32.
18 Hamann D, Yazar K, Hamann C R, Thyssen J P, Lidén C. *p*-Phenylenediamine and other allergens in hair dye products in the United States: a consumer exposure study. *Contact Dermatitis* 2014: **70**: 213–218.
19 Søsted H, Basketter D A, Estrada E, Johansen J D, Patlewicz G Y. Ranking of hair dye substances according to predicted sensitization potency: quantitative structure–activity relationships. *Contact Dermatitis* 2004: **51**: 241–254.
20 SCCP (Scientific Committee on Consumer Products). Memorandum on hair dye substances and their sensitising properties, 19 December 2006. 2006. Scientific Committee on Consumer Products.
21 Matsuo Y, Ito A, Masui Y, Ito M. A case of allergic contact dermatitis due to arbutin. *Contact Dermatitis* 2015: **72**: 405–406.
22 Uter W, Lessmann H, Geier J, Schnuch A. Contact allergy to hairdressing allergens in female hairdressers and clients – current data from the IVDK, 2003–2006. *J Dtsch Dermatol Ges* 2007: **5**: 993–1001.
23 Thyssen J P, Andersen K E, Bruze M et al. *p*-Phenylenediamine sensitization is more prevalent in central and southern European patch test centres than in Scandinavian: results from a multicentre study. *Contact Dermatitis* 2009: **60**: 314–319.
24 Schnuch A, Lessmann H, Frosch P J, Uter W. para-Phenylenediamine: the profile of an important allergen. Results of the IVDK. *Br J Dermatol* 2008: **159**: 379–386.
25 Brunn Poulsen P, Strandesen M (Eds). *Survey and Occurrence of PPD, PTD and Other Allergenic Hair Dye Substances in Hair Dyes*: The Danish Environmental Protection Agency, 2013.
26 Benezra C, Maibach H. True cross-sensitization, false cross-sensitization and otherwise. *Contact Dermatitis* 1984: **11**: 65–69.
27 Yazar K. *Consumers, Cosmetics and Skin Sensitizers*: Karolinska Institutet, Stockholm, 2014.
28 Geier J, Lessmann H, Schnuch A, Hildebrandt S, Uter W. Patch testing with *p*-toluene diamine preparations of different ages. *Contact Dermatitis* 2005: **53**: 75–79.
29 Peters K-P, Frosch P J, Uter W et al. Typ IV-Allergien auf Friseurberufsstoffe. Ergebnisse einer multizentrischen Studie in acht Kliniken der Deutschen Kontaktallergiegruppe und des 'Informationsverbundes Dermatologischer Kliniken' in Deutschland. *Derm Beruf Umwelt* 1994: **42**: 50–57.
30 Frosch P J. Aktuelle Kontaktallergene. *Hautarzt* 1990: **41** (Suppl. 10): 129–133.
31 SCCS (Scientific Committee on Consumer Safety). Opinion on resorcinol, 23 March 2010. Scientific Committee on Consumer Safety.
32 Uter W, Lessmann H, Geier J, Becker D, Fuchs T, Richter G. The spectrum of allergic (cross-)sensitivity in clinical patch testing with 'para amino' compounds. *Allergy* 2002: **57**: 319–322.
33 Almeida P J, Borrego L, Pulido-Melián E, González-Daz O. Quantification of *p*-phenylenediamine and 2-hydroxy-1,4-naphthoquinone in henna tattoos. *Contact Dermatitis* 2012: **66**: 33–37.
34 Belhadjali H, Ghannouchi N, Amri C, Youssef M, Amri M, Zili J. Contact dermatitis to henna used as a hair dye. *Contact Dermatitis* 2008: **58**: 182.
35 Nigam P K, Saxena A K. Allergic contact dermatitis from henna. *Contact Dermatitis* 1988: **18**: 55–56.
36 Gupta B N, Mathur A K, Agarwal C, Singh A. Contact sensitivity to henna. *Contact Dermatitis* 1986: **15**: 303–304.
37 Majoie I M, Bruynzeel D P. Occupational immediate-type hypersensitivity to henna in a hairdresser. *Am J Contact Dermat* 1996: **7**: 38–40.
38 Bolhaar S T, Mulder M, van Ginkel C J. IgE-mediated allergy to henna. *Allergy* 2001: **56**: 248.
39 Kanerva L, Jolanki R, Riihimäki V, Kalimo K. Patch test reactions and occupational dermatoses caused by hydrogen peroxide. *Contact Dermatitis* 1998: **39**: 146.
40 Bregnhøj A, Søsted H. Type I ammonium persulfate allergy with no cross reactivity to potassium persulfate. *Contact Dermatitis* 2009: **61**: 356–357.
41 van der Walle H B, Brunsveld V M. Dermatitis in hairdressers. (I). The experience of the past 4 years. *Contact Dermatitis* 1994: **30**: 217–221.
42 Uter W, Geier J, Lessmann H, Schnuch A. Is contact allergy to glyceryl monothioglycolate still a problem in Germany? *Contact Dermatitis* 2006: **55**: 54–56.
43 Uter W, Geier J, Pirker C et al. Ammonium thiolactate and thiolactic acid: important hairdressers' allergens? *Contact Dermatitis* 2002: **46**: 242–243.
44 Assier-Bonnet H, Revuz J. Chloroacetamide as a cause of contact dermatitis in hairdressing. *Contact Dermatitis* 1999: **40**: 284–285.
45 Chow E T, Avolio A M, Lee A, Nixon R. Frequency of positive patch test reactions to preservatives: the Australian experience. *Australas J Dermatol* 2013: **54**: 31–35.
46 Schnuch A, Lessmann H, Geier J, Uter W. Contact allergy to preservatives. Analysis of IVDK data 1996–2009. *Br J Dermatol* 2011: **164**: 1316–1325.
47 Jo J-H, Jang H-S, Ko H-C, Kim M-B, Oh C-K, Kwon Y-W, Kwon K-S. Pustular psoriasis and the Kobner phenomenon caused by allergic contact dermatitis from zinc pyrithione-containing shampoo. *Contact Dermatitis* 2005: **52**: 142–144.
48 de Groot A C, van der Walle H B, Weyland J W. Contact allergy to cocamidopropyl betaine. *Contact Dermatitis* 1995: **33**: 419–422.
49 Angelini G, Foti C, Rigano L, Vena G A. 3-Dimethylaminopropylamine: a key substance in contact allergy to cocamidopropylbetaine? *Contact Dermatitis* 1995: **32**: 96–99.
50 Suuronen K, Pesonen M, Aalto-Korte K. Occupational contact allergy to cocamidopropyl betaine and its impurities. *Contact Dermatitis* 2012: **66**: 286–292.

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

51 Schnuch A, Lessmann H, Geier J, Uter W. Is cocamidopropyl betaine a contact allergen? Analysis of network data and short review of the literature. *Contact Dermatitis* 2011: **64**: 203–211.
52 Aalto-Korte K, Pesonen M, Kuuliala O, Suuronen K. Occupational allergic contact dermatitis caused by coconut fatty acids diethanolamide. *Contact Dermatitis* 2014: **70**: 169–174.
53 Dejobert Y, Delaporte E, Piette F, Thomas P. Eyelid dermatitis with positive patch test to coconut diethanolamide. *Contact Dermatitis* 2005: **52**: 173.
54 Fowler J Jr. Allergy to cocamide DEA. *Am J Contact Dermat* 1998: **9**: 40–41.
55 de Groot A C, de Wit F S, Bos J D, Weyland J W. Contact allergy to cocamide DEA and lauramide DEA in shampoos. *Contact Dermatitis* 1987: **16**: 117–118.
56 Lessmann H, Uter W, Schnuch A, Geier J. Skin sensitizing properties of the ethanolamines mono-, di-, and triethanolamine. Data analysis of a multicentre surveillance network (IVDK) and review of the literature. *Contact Dermatitis* 2009: **60**: 243–255.
57 Schmutz J-L, Barbaud A, Tréchot P. Allergie de contact à la triéthanolamine contenue dans des gouttes auriculaires et dans un shampooing. *Ann Dermatol Venereol* 2007: **134**: 105.
58 Chinuki Y, Takahashi H, Dekio I, Kaneko S, Tokuda R, Nagao M, Fujisawa T, Morita E. Higher allergenicity of high molecular weight hydrolysed wheat protein in cosmetics for percutaneous sensitization. *Contact Dermatitis* 2013: **68**: 86–93.
59 SCCS (Scientific Committee on Consumer Safety). Opinion on the safety of hydrolysed wheat proteins in cosmetic products, submission I, 18 June 2014, SCCS/1534/14, revision of 22 October 2014, 2014. Scientific Committee on Consumer Safety.
60 Vigan M. Les nouveaux allergènes des cosmétiques. La cosmétovigilance. *Ann Dermatol Venereol* 1997: **124**: 571–575.

© 2015 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

Table S1: Substances employed in hair cosmetic series in single departments. All allergens in pet., except where indicated otherwise.

INCI name (or other name, if none exists)	CAS no.	%
p-Phenylenediamine-HCl	624-18-0	0.5
m-Phenylenediamine §	108-45-2	2
o-Phenylenediamine §	95-54-5	2
o-Aminophenol §	95-55-6	1
N-phenyl-*p*-phenylenediamine sulphate	4698-29-7	0.1
1-hydroxy-4-(*p*-toluidino) anthraquinone §	81-48-1	1
4-Benzyloxyphenol §	103-16-2	1
2,4-Diaminophenol-diHCl §	137-09-7	2
2,4-Diaminodiphenylamine §	136-17-4	0.25
4-Hydroxypropylamino-3-nitrophenol	92952-81-3	1
Direct Orange 34 §	12222-37-6	5
Cocamidopropyl dimethylamine (“acidic buffer”)	68140-01-2	0.05, 0.16, 0.5
Triethanolamine	102-71-6	2.5
Diethanolamine §	111-42-2	2

Thiolactic acid	79-42-5	1
Thioglycolic acid (aq.)	68-11-1	0.3
Cysteamine HCl	156-57-0	1
Potassium persulfate (aq.)	7727-21-1	2.5
Benzoyl peroxide	94-36-0	1

§ use currently not permitted in cosmetics (included in Annex II to the Cosmetics Regulation).