ANNEX 1

Response document for MHRA public consultation on the proposal to make Colourstart Test Patch available from general sales outlets without prescription

Ref: ARM 97

Your details
Name: [redacted]

Position (if applicable): President of the British Association of Dermatologists

Organisation (if applicable): British Association of Dermatologists

Email: [redacted] [redacted]

1. Do you consider that Colourstart Test Patch should be available as a General Sale List (GSL) medicine?

No

Please provide any comments or evidence to support your response:

Please refer to detailed attached response.

2. Do you have any specific comments on the leaflet or the label provided in the public reclassification report for Colourstart Test Patch?

Please refer to detailed attached response.

3. Do you have any other comments on the reclassification?

Please refer to detailed attached response.

4. The MHRA may publish consultation responses. Do you want your response to remain confidential?

No

*If partially, please indicate which parts you wish to remain confidential. In line with the Freedom of Information Act 2000, if we receive a request for disclosure of the information we will take full account of your explanation, but we cannot give an assurance that confidentiality can be maintained in all circumstances. Responses to consultation will not normally be released under FOI until the regulatory process is complete.

Responses can be continued onto a separate page if required. This form should be returned by email (reclassification@mhra.gov.uk) to arrive by **7 November 2018.** Contributions received after that date cannot be included in the exercise.

Response to consultation

It is the opinion of the executive committee of the British Society of Cutaneous Allergy (BSCA) and endorsed by the Officers of the Executive Committee of the British Association of Dermatologists (BAD - the designated body representing Consultant Dermatologists in the United Kingdom) that the Colourstart test patch should NOT be available as a General sale list (GSL) medicine.

It is our opinion that a self-conducted consumer test can only be useful if it meets a number of important criteria, including evidence that the test protocol works, that it can and is likely to be used successfully by the consumer or hairdresser, and most importantly that it does not present a significant health risk (e.g. an increased risk of sensitisation and developing allergic reactions from re-exposure).

In short, as with any *in vivo* test, the benefit must outweigh the risks.

Concerns exist in all these areas as detailed below.

Does the Colourstart test patch pose a significant health risk ? - YES

First and foremost the BSCA has concerns that the risks outweigh the benefit of any proposed form of consumer led Allergy Alert Test or the Colourstart 65mcg patch test.

Whilst hair dyes are commonly used, the Cosmetics Directive does not contain an obligation for manufacturers/importers to provide for self-tests or Allergy Alert tests. Rather, Commission Directive 92/86/EEC of 21 October 1992 lifted the obligation to label the warning "sensitivity test advisable before use" for certain hair dyes.

Instead of consumers risking the possibility of becoming sensitized through the use of the Colourstart test patch (or other Allergy Alert Tests) - or of risking a false negative

interpretation and going on to then experience an adverse reaction from being exposed to PPD –alternative strategies have been considered as safer alternatives.

The BSCA is currently in discussion with the Cosmetic Toiletries and Perfumeries Association (CTPA) in the UK to derive such a strategy.

The BSCA would recommend that any consumer reporting an adverse reaction to a hair dye product on its last use, or those reacting adversely to a black henna tattoo, should instead report this to their hairdresser and/or GP and subsequently be referred to a trained Dermatologist for further evaluation, and tests deemed as necessary.

In this way consumers should

a. have more chance of a correct diagnosis
b. obtain accurate information on avoiding exposure to p-paraphenylenediamine (PPD) and other cross reacting chemicals that are found in hair dyes and also not found in hair dyes eg local anaesthetics.
c. be advised of safe alternatives to use to colour their hair.

Leaving aside concerns regarding the use of Allergy Alert Tests in general, there remain significant concerns regarding the Colourstart 65 mcg test patch itself.

The proposal explains that 'in some cases, a medicine may be reclassified directly from prescription only medicine (POM) to GSL, where it meets the necessary requirements and it is safe to do so.

To be reclassified directly from POM to GSL, a medicine must meet both the requirements of POM to Pharmacy medicine (P) and P to GSL reclassification'.

'To be reclassified from POM to P a medicine must

1. be unlikely to be a direct or indirect danger to human health when used without the supervision of a doctor, even if used correctly
2. be generally used correctly (ie not frequently or to a wide extent used incorrectly)'

This proposal concludes that it will be safe to move the Colourstart 65mcg test patch directly from POM to GSL.

The proposal also states that the purpose of the Colourstart 65mcg test patch is *'to determine whether a person is sensitive to PPD by using a small controlled amount of PPD, rather than using an uncontrolled amount, for example with the Allergy Alert Test (AAT), or using nothing at all'.*

The executive committee of the BSCA and the Officers of the Executive Committee of the BAD are of the opinion that comparing this product to other Allergy Alert tests is irrelevant and does not justify that it has any role to play in either identifying PPD allergy for consumers, or justifying its safety.

The documents presented in this application clearly state that *the Colourstart Test 65mcg Cutaneous Patch is indicated for the diagnosis of allergic contact dermatitis to PPD (para-phenylenediamine). Furthermore they state that the reference medicinal product for this application is True Test Panel 2 (Mekos Laboratories AS, Denmark) which was first authorised in the UK on 26 September 1996.*

They also confirm that the Colourstart Test Patch would be the first medicine containing PPD to be available without prescription.

The executive committee of the BSCA and the Officers of the Executive Committee of the BAD are of the opinion that this could pose a threat to the health of consumers.

At present PPD is only available to medically qualified personnel and is used as part of a diagnostic device.

The Colourstart 65mcg Cutaneous Patch is not an innocuous drug. It contains PPD and PPD is categorised as an extreme sensitiser.

At present, the only hair dye substance in the European standard series for patch testing is PPD (at 1% in petrolatum). The preferred test concentration has varied over time and between authors, considering the risk of inducing allergy by patch testing versus the risk of a false-negative result. The concentration has been lowered in some clinics[1], while other experts recommend that the current 1% PPD should be kept[2,3]. PPD has recently been deleted from the standard series in Germany because of the risk of active sensitisation observed from clinical data generated from a number of departments[4].

In cases of suspected severe allergy to PPD a Dermatologist performing patch tests will likely vary the test concentration of PPD – from the usual 1.0% (pet) to 0.1% (pet), or may vary the application time from 48 hours to 12 hours- so as to prevent an unnecessarily severe patch test reaction[5].

It is the opinion of the BSCA and BAD bodies that some patients could therefore expect to develop severe localized bullous reactions to this equivalent 'diagnostic patch test' material. This could result in scarring or long lasting or permanent hypopigmentation or hyperpigmentation. This is in direct contrast to what is stated in the proposal '*This will usually show as a rash, redness and tiny blisters' or 'a positive result is usually seen as a rash, redness and tiny blisters. It may also itch and or feel warm. Note that the redness may not be evenly spread across the area'.*

To make any form of clinical diagnosis, the executive committee of the BSCA and the Officers of the Executive Committee of the BAD are of the opinion that a trained clinician should be involved, and not a member of the public or hairdresser. Current recommendations are that any Dermatologists undertaking patch testing should have at least 6 months' training in a recognised cutaneous allergy training centre, must maintain their expertise, and be performing at least 200 patch tests per annum (Joint BAD/NICE Cutaneous Allergy Services Standards for Accreditation in preparation).

Section 4 Clinical Particulars, and subsection 4.1 Therapeutic Indications, of the Summary of Product Characteristics states that *the Colourstart 65mcg is a screening test for potential allergic contact dermatitis to PPD in people aged 16 years and over.* In other words the medicine is being used as a diagnostic test.

The aforementioned BSCA and BAD bodies share concerns that there is no mention of how this medicine should be used by consumers with regard to frequency of its use.

If it is deemed by the manufacturers to be 'a screening test for potential allergic contact dermatitis to PPD in people aged 16 years and over' then is it the intention that it should be used before each time a hair dye is used?

If not, but it is intended for use in 'screening' for PPD allergy, under what usage conditions should it be applied by consumers?

The aforementioned BSCA and BAD bodies suggest that consumers or hairdressers buying this medicine/diagnostic test require specific advice from the manufacturers in its intended use.

This is a serious omission, but the omission has consequences on the potential risk of active sensitisation caused by the Colourstart Test 65mcg Cutaneous Patch.

The current proposal documents state *'Repeated use leading to sensitisation to PPD, may potentially occur with use of Colourstart Test Patch. Sensitisation to PPD may occur with patch testing. This may also occur with use of the AAT method to detect potential allergy to hair colorant products and with use of hair colourants themselves'*.

The proposal also states that *'the applicant has provided references from the literature and a report written by a consultant toxicologist which confirms that the risk of sensitisation with use of Colourstart Test Patch is 'low'*.

The aforementioned BSCA and BAD bodies are of the opinion that it would be useful to be able to review these references and the report provided by the toxicologist in order to critique further, and in particular under which usage conditions (in particular frequency of use) is the risk of sensitisation considered low.

PPD is categorised as an extreme sensitiser. Experimental studies have clearly shown that the risk of sensitisation increases with allergen dose/unit area, **frequency of exposure**, duration of exposure, occlusion, the presence of penetration enhancing factors and impairment of skin barrier function.

Diagnostic doctor led patch testing (eg using the True Test panel system) is seldom repeated, and if it is it might be only every few years.

Is it intended that individuals colouring their hair will need to repeat this test at least every 4-8 weeks when they use a hair colourant again? This would potentially significantly increase the risk of active sensitisation to PPD[6].

The aforementioned BSCA and BAD bodies recommend that such a risk would

require some form of quantification.

Does the test protocol work ? /'To be reclassified from POM to P a medicine must be generally used correctly (ie not frequently or to a wide extent used incorrectly)'

The aforementioned BSCA and BAD bodies have concerns over the protocol used.

1. Is testing to PPD alone adequate to guarantee a safe hair dye colourant product?

In the proposal, submitted documents state that the Colourstart Test Patch is a test for potential allergy to PPD only.

This is also expressed in Section 4 Clinical Particulars, and subsection 4.1 Therapeutic Indications, of the Summary of Product Characteristics - *the Colourstart 65mcg is a screening test for potential allergic contact dermatitis to PPD in people aged 16 years and over.*

It is estimated that more than two thirds of hair dyes currently contain PPD. However, this also means that approximately one third do not.

Other examples of much used hair dyes, known to be strong or extreme skin sensitisers, are Toluene-2,5-diamine (TDA), 4-Amino-2-hydroxytoluene, and p-Aminophenol.

The Scientific Committee on Consumer Products (SCCP) and the former SCCNFP have recently assessed the dossiers of 46 of the 117 hair dye substances of interest to industry regarding their skin sensitising properties. In a memorandum on hair dye substances and their skin sensitising properties, based on adopted opinions on these 46 hair dye substances, 10 were categorised as extreme, 13 as strong and 4 as moderate skin sensitisers, all fulfilling the EU criteria for classification as a skin sensitiser[7].

This means that although PPD has been used as the screening agent for hair dye contact allergy in the European standard series, and studies confirm that it is an acceptable screening agent, other colouring ingredients,[8-12] a viscosity stabilizer[13] and an antioxidant[14] have all been reported as responsible allergens in allergic contact dermatitis to hair dye products. The U.K. literature also suggests that a growing number of cases of lone TDA sensitization in hairdressers is being observed[15].

In such circumstances, the Colourstart test patch 65mcg would fail to detect an allergic response in these sensitized consumers.

A recent survey of oxidative hair dyes on the Swedish market concluded that the use of a number of potently sensitizing hair dyes is now more prevalent than the use of PPD, and that screening chemicals other than PPD should be incorporated into diagnostic patch test series[16].

Therefore it is inevitable that some cases of sensitisation to hair dyes will be missed

using the Colourstart test patch.

The aforementioned BSCA and BAD bodies are of the opinion that consumers investing in this medicine for its intended purpose should be clearly advised that it may not detect all adverse reactions to hair dyes– especially if the products they are being exposed to do not contain PPD.

Currently the information sheet enclosed with the product states that *'the absence of a reaction following use of Colourstart does not guarantee a safe hair colour treatment, but by following these safety instructions, you can minimise risk'.*

The aforementioned BSCA and BAD bodies are of the opinion that this information is inadequate for all the above reasons, and the limitations of the test patch should be fairly explained to consumers, if it is to be sold on the GSL.

In preference, consumers may find this information expressed as a percentage more helpful.

2. Is the Colourstart test patch technique adequate to detect contact allergy to PPD?

The aforementioned BSCA and BAD bodies have several concerns about the technique for using the Colourstart test patch as currently included in the proposal.

False negative results from "self testing" is considered to be the largest problem. False- negative results may cause harm to consumers, as they may lead to severe clinical reactions due to hair dyeing with substances to which the consumer is allergic.

It is known that different anatomical sites have different sensitivity for diagnostic patch testing, and the upper back is recommended due to best reproducibility and least false-negative results[17]. In a dose-response study with PPD, however, no statistical difference in response was found between the upper back, lateral aspect of the upper arm and behind the ear when read by a skilled observer[18].

However, this was when read by a skilled observer. It is proposed that the Colourstart test patch be 'placed on the upper arm (above the elbow but below the shoulder) where you will be able to see the test results'.

The proposal documents state that *'Incorrect interpretation of the patch test result may occur if an individual is taking medicines such as corticosteroids or immunosuppressants'.*

The package leaflet lists specific drug examples '*prednisolone, betamethasone, fluticasone, hydrocortisone or immunosuppressant medicines (such as tacrolimus, cyclosporine, mycophenolate, azathioprine, sirolimus)'.*

This list is not exhaustive and could be misleading if interpreted literally by members of the public or not understood.

False negative patch test readings can also occur if the site has been exposed to UV radiation (such as a holiday in the sun), or if there is insufficient occlusion or occlusion time.

In summary, there are many variables that can affect the interpretation of diagnostic patch tests which is why they are best left in the hands of a trained and experienced clinician.

Secondly, the package leaflet and information provided for the consumer confuses the issue of when to apply the test patch before considering a colouring process, and when to take readings looking for a positive patch test reaction.

The aforementioned BSCA and BAD bodies are of the opinion that information provided to the consumer on when to apply the patch is also too ambiguous for it to be placed on the general sales list.

The package insert with the test patch states *'Always apply the self-adhesive patch at least 48 hours (2 days) or ideally 5 days before any colouring process'.*

Presumably this is to ensure that any 'positive' reactions are detected and the hair colouring process is not performed, and thereby an allergic response is avoided.

However, this is in contrast to standardised diagnostic patch testing techniques when recommended readings take place between 48 hours, 72 hours and 7 days. This is to give the greatest chance of detecting contact allergy.

Certainly, if the reading time of the Colourstart patch test is restricted to 48 hours, followed by a colouring process, then sensitisation may be missed, since patch test reactions frequently develop up to 7 days after application.

The package leaflet states that *'PPD sensitivity sometimes causes reactions which may not appear until 4 to 5 days after the application. If this occurs seek advice from your doctor'.*

The SPC states *'Although the response can appear as early as six hours, it is believed that the most accurate interpretation may be made between 72 and 96 hours after application since "irritant" reactions will have faded by then'.*

The aforementioned BSCA and BAD bodies are of the opinion that the information provided on the package leaflet is both inadequate and ambiguous, and should instead state that the test should be performed at least a period of 7 days before a colouring process is used. Furthermore, consumers should be made aware of the reasons for this ie that it can take up to 7 days for positive results to appear.

Is the colour test patch likely to be used successfully by the consumer or hairdresser?

The aforementioned BSCA and BAD bodies also have concerns with the 'identifying the results' section of the package insert.

This states that *'a positive result is usually seen as a rash, redness and tiny blisters. It may also itch and or feel warm. Note that the redness may not be evenly spread across the area'. For a negative result 'There should be no visible differences in the two patches marked A+ and A-'.*

Interpreting patch test reactions is difficult. In clinical diagnostic patch testing, readings are undertaken by trained observers. It requires experience and should be performed by dermatologists with adequate training[19-21].

In the proposal documents it is stated that *'the license holder of the test patch has provided results of a clinical study comparing the Colourstart Test Patch with the Finn Chamber (a skin patch test chamber used for patch testing) in detection of PPD allergy in subjects with known or suspected allergy and those with no known allergy to PPD. There were recruitment difficulties with this study, in part possibly due to increased media attention alerting potential participants to the risk of severe allergic reaction to ingredients in hair colourants. However, the study demonstrated that participants were able to identify allergy, if present, and in general took a more conservative approach to interpreting the patch test result than the study investigators. Adverse events were mainly mild in nature and, in most cases, resolved without treatment'.*

The aforementioned BSCA and BAD bodies are not aware of this study's having being published in a peer reviewed journal, or whether it has any statistical power, and believe that the results should be made available for scrutiny before this medicine is considered for being made available on the general sales list.

In a previously published paper, difficulties with consumer led interpretation of a self applied patch test device have been described[22.] .

<u>Is the Colourstart test patch suitable for a General Sale List (GSL) Medicine with availability in general sales outlets ?</u>

The aforementioned BSCA and BAD bodies have concerns about both of these proposals and in particular the knowledge base about PPD amongst pharmacists and General Practitioners.

The proposed documents state that for a medicine to be classified as GSL it must also be demonstrated that it **does** meet the GSL criterion, which is set out in the Human Medicines regulations 2012, regulation 62(5). This criterion is as follows:

`GSL may be appropriate for medicines which can, with reasonable safety, be sold or supplied otherwise by or under supervision of a pharmacist.'

The aforementioned BSCA and BAD bodies are not aware of any evidence that Pharmacists receive specific training on type 4 hypersensitivity reactions to hair dye colourants and their constituents including PPD.

In fact it is well known that GPs and other medical practitioners receive very little training in Dermatology and type 4 hypersensitivity reactions including to hair dye colourants. This is borne out by testimony from patch test clinicians who frequently encounter patients who have been misdiagnosed and suboptimally treated following allergic reactions to PPD from hair colourant exposure.

The proposed documents also state that:

'Individuals purchasing and intending to use Colourstart Test Patch will be aware of the risks associated with the use of hair colourants and the need to test for potential allergy to hair colourants prior to use. Advice of a pharmacist is not considered necessary for the consumer to purchase Colourstart Test Patch for its intended use'.

Availability of Colourstart Test Patch in hairdressing salons or other outlets where hair colourants are sold is considered appropriate. Most hair colourants are purchased outside pharmacies and the ATT test is undertaken without advice from a pharmacist. Limiting Colourstart Test Patch to pharmacy (P) legal status would unnecessarily limit the availability of the test.'

However, the proposed package leaflet makes 9 references to consumers talking directly to their 'doctor' or 'pharmacist' and there is 1 such reference in the SPC.

This includes advice as to whether the product is suitable for use in a particular individual consumer eg concurrent immunomodulating medicines (1), and advice on interpretation of the test using this medicine (4,6,7).

List of references to speaking to a 'doctor or pharmacist printed on proposal documents

1. *Talk to your doctor or pharmacist before using Colourstart if any of these factors apply to you. Your doctor or pharmacist will be able to decide what to do.*
2. *If this happens talk to your doctor or pharmacist and **DO NOT** use hair colorants if this happens.*
3. *If you are pregnant or think you might be pregnant or are planning to have a baby ask your doctor or pharmacist for advice before taking this medicine.*
4. *If you experience any symptoms of discomfort or there is a noticeable difference in how your skin looks or feels in this 48 hour period, remove the patch and wash the area gently with water as it may be a positive result. **DO NOT** apply hair colorant. Talk to your pharmacist or doctor if you are at all unsure.*
5. *If a severe patch test reaction develops which is seen as redness with large fluid filled blisters, talk to your doctor immediately. DO NOT apply hair colorant.*
6. *PPD sensitivity sometimes causes reactions which may not appear until 4 to 5 days after the application. If this occurs seek advice from your doctor.*
7. *If you have any further questions on the use of this medicine, ask your doctor or pharmacist.*
8. *If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.*

The aforementioned BSCA and BAD bodies are of the opinion that if there is no supporting evidence that Pharmacists receive specific training regarding the use of hair colourants and PPD, or patch testing as a diagnostic test, then this clearly contrasts with the criteria for GSL.

Equally, if there is no supporting evidence that General Practitioners receive specific training regarding the use of hair colourants and PPD, or patch testing as a diagnostic test, there will be no help available to consumers when they approach their GPs.

The proposal documents argue that '*most hair colourants are purchased outside pharmacies and the ATT test is undertaken without advice from a pharmacist'*.

However, this bears no relation to concerns that the Colourstart patch test is a medicine and at the same time an equivalent diagnostic device.

The aforementioned BSCA and BAD bodies oppose the view that 'limiting the Colourstart Test Patch to pharmacy (P) legal status would unnecessarily limit the availability of the test.'

It is the view of the BSCA and BAD that convenience must never supercede safety concerns.

Summary from another Expert Panel

Three independent non-food Scientific Committees provide the European Commission with the scientific advice it needs when preparing policy and proposals relating to consumer safety, public health and the environment. The Committees also draw the Commission's attention to the new or emerging problems which may pose an actual or potential threat.

These include the SCCP.

For the past two decades, European members states, in response to calls from Dermatologists, have raised concerns at possible risks arising from Allergy Alert Tests[23]

The SCCP adopted an opinion on 'sensitivity to hair dye- consumer self testing' at its 14thplenary meeting on 18 December 2007[24].

In the opinion, the SCCP stated the following:

- Sensitivity testing "should be performed by adequately trained dermatologists who will be medico-legally responsible for any problems related to false negative results and active sensitisation,

and who are trained to evaluate any response and can give advice accordingly.

It concluded the following points

- There is a potential risk that "self tests" may result in induction of skin sensitisation to hair dye substances.

- There is a risk that "self tests" with hair dye products and with separate kits may lead to misleading and false-negative results, thus giving individuals who are allergic to hair dye substances the false impression that they are not allergic or not at risk of developing an allergic reaction by dyeing their hair.

Conclusion

The license holder wishes to market a diagnostic patch test allergen directly to consumers for the purposes of detecting PPD sensitisation and preventing allergic reactions. The license holder argues that this test patch has advantages over what is currently suggested by hair dye manufacturers to use as an Allergy Alert test.

The aforementioned BSCA and BAD bodies fully endorse concerns raised by Dermatologists over the use of any Allergy Alert tests or the Colourstart test patch 65mcg from several major perspectives:

1. the risk to human health of inducing sensitisation to PPD from frequent and inappropriate use (thereby causing cosensitisation to other drugs such as local anaesthetics)

2. the risk to human health arising from the failure to detect PPD and other hair colourant allergens (false negative reactions)

3. the risk to human health from members of public failing to properly use a diagnostic device intended by its manufacturer for use by trained clinicians.

The proposal documents explain that for a medicine to be classified as P it must **not** meet any of the criteria for POM classification, which are set out in the Human Medicines Regulations 2012, regulation 62(3).

These criteria include: A direct or indirect danger existing to human health, even when used correctly, if used without medical supervision.

For all of the above stated reasons, the executive committee of the British Society of Cutaneous Allergy (BSCA) and endorsed by the Officers of the Executive

Committee of the British Association of Dermatologists do not endorse that the Colourstart test patch 65mcg should be available as a General sale list medicine

[redacted]

[redacted]

President of the BSCA

On behalf of the Executive Committee BSCA

07/11/2018

[redacted]

[redacted]

President of the BAD

On behalf of the Officers of the Executive Committee BAD

References

1. Aalto-Korte K, Alanko K, Kuuliala O, Jolanki R. Late reactions in patch tests: a 4-year review from a clinic of occupational dermatology. Contact Dermatitis 2007;56:81–86.

2. Gawkrodger DJ, English JSC. How safe is patch testing to PPD? Br J Dermatol 2006;154:1025–1027.

3. McFadden JP, White IR, Johansen J, Bruze M. Should para-phenylenediamine (PPD) 1% pet. be part of commercially available standard series? Contact Dermatitis 2005;53:183–184.

4. Schnuch A, Becker D. DKG Nachrichten. Die Deutche Kontaktallergie Gruppe informiert. Dermatologie in Beruf und Umwelt 2005;53:98-99.

5. JM Hextall, NJ Alagaratnam, AK Glendinning et al Dose–time relationships for elicitation of contact allergy to *para*-phenylenediamine. Contact Dermatitis 2002;47:96-99.

6. White JM, Basketter DA, Pease CK, Sanders DA, McFadden JP. Intermittent exposure to low-concentration paraphenylenediamine can be equivalent to single, higher-dose exposure. Contact Dermatitis. 2007;56:262-5.

7. SCCP/1054/06 Memorandum on Hair dye substances and their skin sensitising properties. Adopted by the Scientific Committee on Consumer Products (SCCP) during

the 10th plenary of 19 December 2006.

8. Blanco R, de la Hoz B, Sa´nchez-Ferna´ndez C, Sa´nchez-Cano M. Allergy to 4-amino-3-nitrophenol in a hair dye. Contact Dermatitis 1998; 39:136.

9. Wedi B, Hoting E, Koerner M et al. Allergic contact dermatitis due to monovalent sensitisation to the oxidation hair dye intermediate oxamitol (2-amino-methyl-p-aminophenol-2-HCl) without cross sensitivity to haptens of the para-group. Contact Dermatitis 2000; 42:104–5.

10. Eskelinen A, Molitor C, Kanerva L. Allergic contact dermatitis from 2,7-dihydroxynaphthalene in hair dye. Contact Dermatitis 1997; 36:312–13.

11 Le Coz CJ, Ku¨hne S, Engel F. Hair dye allergy due to 3-nitro- p-hydroxyethyl-aminophenol. Contact Dermatitis 2003; 49:103.

12 Sosted H, Menne´ T. Allergy to 3-nitro-p-hydroxyethyl-aminophenol and 4-amino-3-nitrophenol in a hair dye. Contact Dermatitis 2005; 52:317–19.

13 Bowling JCR, Scarisbrick J, Warin AP et al. Allergic contact dermatitis from trideceth-2-carboxamide monoethanolamine (MEA) in a hair dye. Contact Dermatitis 2002; 47:116–17.

14 Le Coz CJ, Schneider GA. Contact dermatitis from tertiary-butyl- hydroquinone in a hair dye, with cross sensitivity to BHA and BHT. Contact Dermatitis 1998; 39:39–40.

15 Winhoven SM, Rutter KJ, Beck MH. Toluene-2,5-diamine may be an isolated allergy in individuals sensitized by permanent hair dye. Contact Dermatitis 2007; 57:93.

16 Yazar K, Boman A, Lide´n C. Potent skin sensitizers in oxidative hair dye products on the Swedish market. Contact Dermatitis 2009: **61**: 269–275.

17 Wahlberg JE, Lindberg M. Patch testing (Chapter 22). In: Contact Dermatitis 4th edn. (textbook). Eds: Frosch PJ, Menné T, Lepoittevin J-P. Springer-Verlag, 2006, 365-390.

18 Søsted H, Menné T, Johansen JD. Patch test dose–response study of p-phenylenediamine: thresholds and anatomical regional differences. Contact Dermatitis 2006;54:145–149.

19 Aberer W, Andersen KE, White IR. Should patch testing be restricted to dermatologists only? Contact Dermatitis 1993;28:1-2.

20 Lindberg M, Bruze M. Patch tests should be performed by experienced dermatologists. Many allergens can cause contact dermatitis. Läkartidningen 1995;92:3673-3675. [Article in Swedish]

21 Wahlberg JE, Lindberg M. Patch testing (Chapter 22). In: Contact Dermatitis 4th edn. (textbook). Eds: Frosch PJ, Menné T, Lepoittevin J-P. Springer-Verlag, 2006, 365-390.

22 Orton D. A UK study on the use of and reported adverse reactions to hair dyes. Contact Dermatitis 2008: 58: 27–28.

23 Orton D, Basketter D. Hair dye sensitivity testing: a critical commentary. Contact Dermatitis 2012: 66: 312-16.

24 Scientific Committee on Consumer Products opinion on: Sensitivity to Hair Dyes - Consumer Self Testing. Adopted by the SCCP during the 14th plenary meeting on 18 December 2007