

**Risk Management Option Analysis Conclusion Document**

**Substance Name: p-phenylenediamine**

**EC Number: 203-404-7**

**CAS Number: 106-50-3**

**Authority: RIVM**

**Date: December 2017**

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# Foreword

The purpose of Risk Management Option analysis (RMOA) is to help authorities decide whether further regulatory risk management activities are required for a substance and to identify the most appropriate instrument to address a concern.

RMOA is a voluntary step, i.e., it is not part of the processes as defined in the legislation. For authorities, documenting the RMOA allows the sharing of information and promoting early discussion, which helps lead to a common understanding on the action pursued. A Member State or ECHA (at the request of the Commission) can carry out this case-by-case analysis in order to conclude whether a substance is a 'relevant substance of very high concern (SVHC)' in the sense of the SVHC Roadmap to 2020[[1]](#footnote-1).

An RMOA can conclude that regulatory risk management at EU level is required for a substance (e.g. harmonised classification and labelling, Candidate List inclusion, restriction, other EU legislation) or that no regulatory action is required at EU level. Any subsequent regulatory processes under the REACH Regulation include consultation of interested parties and appropriate decision making involving Member State Competent Authorities and the European Commission as defined in REACH.

This Conclusion document provides the outcome of the RMOA carried out by the author authority. In this conclusion document, the authority considers how the available information collected on the substance can be used to conclude whether regulatory risk management activities are required for a substance and which is the most appropriate instrument to address a concern. With this Conclusion document the Commission, the competent authorities of the other Member States and stakeholders are informed of the considerations of the author authority. In case the author authority proposes in this conclusion document further regulatory risk management measures, this shall not be considered initiating those other measures or processes. Since this document only reflects the views of the author authority, it does not preclude Member States or the European Commission from considering or initiating regulatory risk management measures which they deem appropriate.

### OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

|  |  |  |
| --- | --- | --- |
| RMOA |  | Risk Management Option Analysis (RMOA) other than this RMOA |
| REACH Processes | Evaluation | Compliance check, Final decision |
| Testing proposal |
| CoRAP and Substance Evaluation |
| Authorisation | Candidate List |
| Annex XIV |
| Restri-ction | Annex XVII[[2]](#footnote-2) |
| Harmonised C&L |  | Annex VI (CLP) (see section 3.1) |
| Processes under other EU legislation |  | Plant Protection Products Regulation  Regulation (EC) No 1107/2009 |
|  | Biocidal Product Regulation  Regulation (EU) 528/2012 and amendments |
| Previous legislation |  | Dangerous substances Directive  Directive 67/548/EEC (NONS) |
|  | Existing Substances Regulation  Regulation 793/93/EEC (RAR/RRS) |
| (UNEP) Stockholm convention (POPs Protocol) |  | Assessment |
|  | In relevant Annex |
| Other processes/ EU legislation |  | Other (provide further details below) |

Remarks on Table 2:

### Restriction proposal

ECHA is currently developing a proposal for restricting CMRS substances in tattoos and permanent make-up. Submission of the proposal is expected medio 2017. The Swedish Competent Authority on REACH is developing a restriction proposal for skin sensitizers in textile.

### Testing proposal

Testing proposal for Long-term toxicity testing in fish. Deadline for submitting the information was 14/03/2011. No dossier nor any other information was available on the ECHA home page.

The Registrant proposes to conduct acute and chronic studies in *Daphnia* first as well as in algae (see testing proposals for acute and chronic toxicity to aquatic invertebrates and testing proposals for toxicity to aquatic algae), under conditions in which the concentration of PPD is kept as constant as possible. A fully validated analytical method is under development for that purpose. It is stated that “*It may be possible to demonstrate with the outcome of this study and the existing data that fish are not the most sensitive trophic level and that chronic fish studies are not required”*. This would be in accordance with the Guidance on information requirements and chemical safety assessment chapter R.10: Characterisation of dose [concentration]-response for environment and table R.10-4 assessment factors to derive a PNECaquatic will be used: “if it is possible to determine with high probability that the most sensitive species has been examined, i.e. that a further long-term result from a different taxonomic group would not be lower than the data already available, a third NOEC will not need to be determined in those circumstances, a factor of 10 applied to the lowest long term result (e.g. EC10 or NOECs) from only two species is also appropriate”. If the planned studies show that this is indeed the case, the registrant will ask ECHA to deny permission for this chronic fish study.

### Other regulations

#### Cosmetics regulation (EC) no. 1223/2009

In the Cosmetics Regulation (EC) no. 1223/2009, p-phenylenediamine is mentioned in ANNEX III, entry 8: List of substances which cosmetic products must not contain except subject to the restriction laid down. Entry 8 suggests that p-phenylene diamine is not allowed for use in cosmetics other than the onces indentified below. Article 2(1a) and 2(1b) of this Regulation defines a cosmetic product as:

*2(1a) ‘cosmetic product’ means any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odours;*

*2(1b) ‘substance’ means a chemical element and its compounds in the natural state or obtained by any manufacturing process, including any additive necessary to preserve its stability and any impurity deriving from the process used but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition;*

It is furthermore stated under (8) of the Regulation that:

*The Commission should define the categories of cosmetic products which are relevant for the application of this Regulation.*

(Black) Henna tattoos are not mentioned in the list of possible cosmetic products included under (7) of the Regulation. The manual on borderline cases for cosmetic products (2017)[[3]](#footnote-3) makes note of washable, temporary tattoos (section 1.5) suggesting that these might meet the criteria for being a cosmetic product. Consultation of the Dutch Authority for food and product safety learns that (Black) Henna Tattoos indeed meet the criteria of a cosmetic product as line out under article 2(1a) and are to be considered as such. By Annex III, entry 8 of the Regulation does imply that p-phenylene diamine is not allowed for use in temporary tattoos like e.g. (black) Henna tattoos.

Hair dye in oxidative hair products, Annex III entry 8a

Thus the use of p-phenylenediamine and its salts is restricted to hair dye substance in oxidative hair dye products for general and professional use. For both uses, the maximum concentration applied to hair must not exceed 2% calculated as free base after mixing under oxidative conditions.

The warnings are that:

*Hair colourants can cause severe allergic reactions. Read and follow instructions. This product is not intended for use on persons under the age of 16. Temporary “black henna” tattoos may increase your risk of allergy. Do not colour your hair if: — you have a rash on your face or sensitive, irritated and damaged scalp, — you have ever experienced any reaction after colouring your hair, — you have experienced a reaction to a temporary “black henna” tattoo in the past. Contains phenylenediamines. Do not use to dye eyelashes or eyebrows.’*

Products for eyelashes colouring, Annex III entry 8b

Products intended for colouring eyelashes for professional use only with the same warnings as written above.

#### Other regulations

Other regulations and directives that could possibly include a specific note on p-phenylenediamine but in which this substance is not explicitely mentioned are:

1. Regulation (EU) no. 1007/2011 on textile fibre names and related labelling and marking of the fibre composition of textile products
2. DIRECTIVE 2001/95/EC on general product safety
3. DIRECTIVE 2009/48/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 June 2009 on the safety of toys

### CONCLUSION OF RMOA

This conclusion is based on the REACH and CLP data as well as other available relevant information taking into account the SVHC Roadmap to 2020, where appropriate.

|  |  |
| --- | --- |
| **Conclusions** | **Tick box** |
| Need for follow-up regulatory action at EU level: |  |
| *Harmonised classification and labelling* | X |
| *Identification as SVHC (authorisation)* |  |
| *Restriction under REACH* | X |
| *Other EU-wide regulatory measures* |  |
| Need for action other than EU regulatory action | CCH |
| No action needed at this time |  |

### Need for follow-up regulatory action at EU level

# Justification for the risk management option

## Need for (further) risk management

An overview of different uses and regulatory risk management measures in place is provided in the table below:

Table 13 Overview of regulatory measures already in place for the different uses identified for PPD

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **OSH** | **Cosmetics Regulation** | | **REACH Restriction** | |
|  |  | Workers | consumers | Sens in textiles | CMRS in tattoos (+) |
| Cosmetics products (overall) | Not applicable | Generally prohibited | Generally prohibited |  |  |
| Hair dye and eyelashes colouring ingredients | Not applicable  Concern for risk for Hairdressers and beautyworkers | Restricted, signals in literature that RM may be insufficient | Restricted, signals in literature that RM may be insufficient |  |  |
| Black henna tattoos | Not applicable | Prohibited | Prohibited  Concern for risk from “holiday” applications obtained outside Europe |  | Black henna tattoos are a cosmetic product and hence most likely out of scope |
| Dye ingredient in textiles, furs and leather | Yes |  |  | May be (partly) in scope (e.g. fur, leather) |  |
| Ink | Yes  Concern for risk for printers |  |  |  |  |
| Photodeveloping agent | Yes  Concern for risk for printers |  |  |  |  |
| Vulcantization accelerator and antioxidant in rubber compounds | Yes |  |  |  |  |
| Monomer for PPTA polymer | Yes |  |  |  |  |
| Intermediate | Yes |  |  |  |  |
| Antioxidant in fuel -refinery | Yes |  |  |  |  |

The various concerns identified for PPD are summarized as follows:

* p-Phenylenediamine is used in dyes to colour hair, eyelashes, skin, textiles, furr and leather, in inks, as a photodeveloper and as a parent compound in vulcanization accelerators and in antioxidants for rubber industry. It is also used in the production of dyes other than hair dyes.
* Effects of p-phenylenediamine can be severe and long-lasting. Especially after high dose exposure leading to elicitation.
* Positive findings from genotoxicity studies in vivo/in vitro of PPD in combination with couplers[[4]](#footnote-4) and /or hydrogen peroxide as well in a carcinogenicity study were reported. The SCCP is of the opinion that the information submitted is insufficient to allow a final risk assessment to be carried out. Before any further consideration, additional data would be required on in vivo genotoxicity and/or carcinogenicity of PPD in combination with hydrogen peroxide and couplers (to simulate consumer exposure). Further information is needed in supporting the applicant’s view that the MoS are sufficiently high.
* For workers, a known association between PPD sensitization cases and hairdressing/beauty occupation exists. Other occupations for which indications for such a positive association are found in literature are bar maids/waiters, cleaners, bakers, household workers and printers.
* For consumers, there is a special concern of exposure via black henna tattoos that may contain high concentrations of PPD. Other, more lower dose exposures through the use of hair dyes or from wearing textile containing PPD dyes may also be of concern.
* For consumers (and workers) there is concern with regard to self-tests for PPD allergy available on the market.

Cross-sentisization has been described:

* to other hair dyes of which at least:
  + toluene-2,5-diamine (lower sensitization potency but used in higher tonnage, see Table 8),
  + p-aminophenol (higher sensitization potency but used in lower tonnage, see Table 8),
  + 2-nitro-PPD (prohibited regulation Cosmetics)
  + disperse orange 3
  + to the black rubber chemical family, including IPPD (N-Isopropyl-N’-phenyl-p-phenylenediamine (cas 101-72-4) antioxidant and antiozonant for natural and synthetic elastomers and as an antiflex agent for the protection against catalytic degradation by copper and other heavy metals.
  + to substances in textile dyes, leather dyes and fur dyes
  + 4-methyl-m-phenylenediamine (2,4-TDA; high rate (67.5%) of cross sensitisation to 2,4-TDA)

Cross-sensitization to other hair dyes beyond the ones identified above is a largely unknown area. For example: 4-amino-2-hydroxytoluene, 2-methyl-5-hydroxyethylaminophenol and 2-methylresorcinol, 4-amino-3-nitrophenol are predicted to be potential cross-sensitizing agents but are not used for patch testing in patients, who have been exposed to hair dyes.

With regard to the development of the prevalence of PPD contact allergy over time there are indications that the prevalence may be increasing Fall et al. (2015) show that the prevalence of PPD contact allergy has been increasing in Sweden over the period 1992-2009. As is summarized in section 3, the use of black henna tattoos is shown to be an important risk factor in the development of PPD contact allergy.

Table 2**: SVHC Roadmap 2020 criteria**

|  |  |  |
| --- | --- | --- |
|  | Yes | No |
| a) Art 57 criteria fulfilled? | Uncertain: skin sensitization may meet 57(f) | |
| b) Registrations in accordance with Article 10? | X |  |
| c) Registrations include uses within scope of authorisation? | X |  |
| d) Known uses not already regulated by specific EU legislation that provides a pressure for substitution? | X |  |

## Identification and assessment of risk management options

### Compliance check

Several compliance issues are identified for PPD that relate to exposure and use information (see section 4). If a Substance Evaluation will be started to obtain further information on health hazards, a request for further information could be considered at the level of the compliance check. However, as a first step is suggested to obtain further insight in uses and exposure through direct and informal contact with the Registrant.

### Occupational safety and health Directive

Worker-groups for which concern was identified include hairdressers and beautyworkers, bar maids/waiters, cleaners, bakers, household workers and printers, and one case from the rubber industry (personal communication). For printers, this potential for a positive association may be influenced by part of the group working with PPD containing inks. For the other worker-groups occupational exposure to PPD-containing products is less clear and sensitization may involve the use of PPD containing cosmetics by those worker-groups. The occupational safety and health Directive applies for all workplaces where PPD is produced, handled or used in mixtures, with the exception of handling cosmetic products. The most appropriate regulatory framework to regulate safe working conditions for handling cosmetics products by workers is a topic of ongoing discussions. At present, safe working conditions for cosmetic products are dealt with under the Cosmetics Regulation (see section 5.2.3).

Under the OSH Directive, there are no specific requirements for working safely with (skin) sensitizers (this is unlike carcinogens, mutagens or reproductive toxic substances). Also under OSH, no limit value for dermal exposure is derived, and PPD has not been given a skin notation to signal its concern for demal exposure. Exposure reduction though, is central to OSH (via the occupational hygienic strategy). Whether the signals for the development of occupational health cases among bar maids/waiters, cleaners, bakers, household workers, printers and the rubber industry orginates from a consumer use of PPD containing products or is initiated by occupational exposure through accidental (high) exposure, because the measures implemented are not sufficient to organize a safe work envrionment, or because the measures are not sufficienty enforced is unclear.

Development of Best available techniques (BAT) in the different sectors in which PPD is produced and used could be considered to reduce exposure as much as possible and manage possible risks from PPD under OSH.

### Cosmetics Regulation

PPD is already restricted for its use in cosmetic products by Annex III, entry 8a and 8b of the Cosmetics Regulation. Through this entry, PPD is restricted to use in oxidative hair dye products for general and professional use and products intended for colouring eyelashes for professional use only. These uses where assessed as by the SCCS (2006) concluding the following:

*“ For the final safety assessment of PPD several aspects have to be taken into account:*

* *The SCCP considers PPD alone as being not genotoxic. But, positive findings from genotoxicity studies in vivo/in vitro of PPD in combination with couplers and /or hydrogen peroxide as well in a carcinogenicity study were reported.*
* *The generally accepted approach (MOS approach) according to the Notes of Guidance results in a MoS of 77. However, when toxicokinetic studies are considered, a minimum MoS of 25 can be set. A number of toxicokinetic studies were performed and the applicant proposed to base the safety on the comparison of AUCs (area under curve). In this approach, the AUC in rats following a peroral dosage of 4 mg/kg (corresponding to the NOAEL) was compared to the AUC in humans following application of a hair dye containing 14C-labeled PPD. In this case a safety margin of 16.3 was obtained which is not considered sufficient by the SCCP.*
* *On the other hand, experimental evidence was provided that PPD is metabolised in the skin to acetylated (i.e. detoxified) derivatives and, furthermore, that presumably activation of PPD (formation of monoxygenated derivatives) does not occur.*

*The SCCP is of the opinion that the information submitted* ***is insufficient to allow a final risk assessment*** *to be carried out. Before any further consideration,* ***additional data would be required on in vivo genotoxicity and/or carcinogenicity of PPD in combination with hydrogen peroxide and couplers*** *(to simulate consumer exposure).* ***Further information is needed in supporting the applicant’s view that the MoS is sufficiently high.****There is an increasing use of hair dyes by young people and additional exposure to PPD-related substances from temporary tattoos and clothing textiles.* ***PPD is an extreme sensitiser and the risk of allergy occurring in the consumer should be realised****.”*

The present analysis indicates that both worker and consumer cases continue to develop. Workers that are most effected include hairdressers and beauty workers.

Takkouche et al (2009) noted that the absence of labelling information required for other chemicals is most often not required for products used by heardressers and beautyworkers which increases potential hazard in subjects frequently exposed to them. Further, this study notes that detection and prevention measures related to industrial hygiene were not instituted in hairdressing and nail care salons before approximately 10 years and were still no common practice as research suggests that little hairdresser salons have appropriate ventilation systems and only about one-third of hairdressers in Nordic countries may still use protective gloves while using hair dyes by the time of publication. Although this study dates from 2009, it is well likely that a similar situation is still found in many hairdresser and beautiworker workplaces.

Comments received at the RiME-II 2017 meeting suggest that wearing protective gloves has become standard over the last years. It should nevertheless be noted that exposure of hairdressers and beauty workers may take place at various moments in the process of using hairdyes or dyes for eyelashes, i.e. during preparation, application, rinsing of the treated hair/lashes, cleaning of the uses tools…. It was suggested at the RiME-II 2017 meeting that exposure reducing measures like wearing gloves might be implemented during preparation and application, but no longer during e.g. rinsing and cleaning activities.

*Based on the remaining occurrence of work related health cases and, to a lesser extend also consumer cases, it is questioned if the current restriction for use under the Cosmetics Regulation is sufficiently protective (= 2% maximum concentration before mixing with an oxidative agent; warning not to exposre oneself when a reaction is observed previously after using a hair dye or black henna tattoo, or when the skin is sensitive or may not be fully intact). Or, if enforcement of safe work practices, intended use by consumers and product composition is sufficient.*

Possible activities that may strengthen the implementation of safe workpractices could be the development of sector specific Best Available Techniques or Best practices development via the channels of the European Social Dialogue. Whether or not developments in these directions could be suited to further improve the current situation should be evaluated in direct contact with the sector in particular for hairdressers and beauty workers.

As the most recent SCCS opinion on PPD stems from 2006 and as concern for safe use was flagged in this opinion, one may consider addressing this issue by informing the Secretariat of the Cosmetics Directive at DG Grow about the continuous concern for safe use of this substance for workers and consumers (at the presently allowed 2% concentration level) being an extreme skin sensitizer and a possible carcinogenic in combination with hydrogen peroxide and couplers. In a follow-up step, the Commission can then demand from the industry to update their dossier for safe use of PPD for workers and consumers, which will be re-evaluated by the SCCS to come to an updated opinion. One limitation of this route is that any information to be newly generated will be confined to non-animal testing. In an updated opinion, further attention could be given to the possibility by workers and consumers to identify PPD containing products (e.g. through labelling) and to using the appropriate protective measures (e.g. by supplying gloves in the packaging).

In addition, over the last years, black henna tattoos are signaled as a potentially important source of concern that calls for further regulation, especially for consumers developing a PPD allergy. It is flaged that the combined exposure to oxidative hair dyes and black henna tattoos may alarmingly increase the chance to become sensitized, already upon a single application such tattoo.

The use of PPD is already restricted for use in cosmetic products by Annex III, entry 8a and 8b of the Cosmetics Regulation. Being not injected subcutaneously, Black henna tattoos are considered a cosmetic product as they meet the definition according to article 2(1a) of the Regulation. Annex III entry 8 thereby implies that the use of PPD in Black henna tattoos is prohibited via the Cosmetics Directive. Consequently, occurrence of PPD in black henna tattoos and concern for consequent health effects is to be addressed through enforcement of the Cosmetics Regulation. However, no Commission decision on whether or not to identify henna tattoos as cosmetic product as specified under (8) of the Regulation could be found and it may be desirable to have such decision to facilitate enforcement.

Information from the Netherlands and Norway on consumer cases suggests that consumer exposure to PPD through application of Black henna tattoos seems primarily a ‘holiday concern’. It is uncertain to what extent this ‘holiday concern’ is located within the EU or relates solely to holiday destinations outside Europe.

### Substance evaluation

PPD may have carcinogenic effects when exposure occurs in combination with a coupler and/or an oxidative agent. This is suggested by positive results reported from genotoxicity studies in vivo/in vitro of PPD in combination with couplers and /or hydrogen peroxide as well in a carcinogenicity study. The SCCP is of the opinion that the information that was submitted at the time of the PPD assessment (in 2006) is insufficient to allow a final risk assessment on carcinogenicity to be carried out. Before any further consideration, additional data would be required on in vivo genotoxicity and/or carcinogenicity of PPD in combination with hydrogen peroxide and couplers (to simulate consumer exposure). To date, this information has not been generated and further information is needed to support the applicant’s view that the MoS are sufficiently high. It is unlikely that this information will be generated in the context of the Cosmetics Directive as this Directive does no longer allow animal testing.

Takkouche et al (2009) performed a meta-analysis of cancer incidences in hairdressers, beautyworkers and related occupations and found a significant increased relative risk in these worker populations in the US and EU in several anatomic sites: 62% for multiple myeloma, 52% for larynx, 30% for bladder and 27% for lung cancer. The analysis was not set up to attribute this increased risk to exposure to specific chemicals, but does suggest that exposure to chemicals at the workfloor, including hairdye products, nitrosamine, acetone, formaldehyde and methacrylates is a likely cause of the observed increased relative risk.

Further information could be requested through the REACH process of Substance Evaluation. When more information is requested through Substance Evaluation, an additional request with regard to use and exposure could be considered also. However, as the available studies that show negative results on carcinogenicity are judged of good quality, it is questionable if new data will provide further insight. If any, further data generation is suggested to focus on the potential incoherence of available test data.

### Classification and Labelling (CLP)

PPD has a harmonized classification for Skin Sensensitization Cat.1. The CSR bases its risk assessment on an LLNA study with an EC3 of 0.06%. This suggests that PPD may meet the criteria for classification as Skin Sens 1A (CLP upper limit boundary for Cat.1A classification is set at an EC3 of 2%). Once PPD would be classified as Skin Sens 1A, the indication of its presence in mixtures will shift from 0.1% (Cat.1) to 0.01% (Cat.1A). Furthermore, the available information on sensitizing effects of PPD may further motivate the derivation of a Specific concentration limit. This change in classification would not directly impact measures under the Cosmetics Regulation, but is expected to impact the communication on hazards of PPD to consumers and workers for the other uses.

Setting a more stringent classification will not impact cosmetic uses as these are exempted from the Classification and Labeling requirements under CLP. It may however impact worker safety at those workplaces where formulation of cosmetics takes place. For use in cosmetics, the maximum concentration limit is set at 2% (before mixing with an oxidative agent). It could therefore be anticipated that the current limit of identification of PPD in mixtures of 0.1% may already be sufficiently low to communicate on PPD containing mixtures at the workfloor. However, actual concentrations handled at the workfloor are unknown. For the other sectors like the rubber, ink and textile industry, PPD concentrations handled at the workfloor are uncertain too. It is therefore not known if lowering the GCL/SCL for PPD will impact the information flow to workers about mixtures containing this substance. However, even when concentrations of PPD in mixtures at the workfloor already exceed the current GCL or SCL due to the CLH as Skin Sens 1, there may still be added value in communicating concentrations based on an even lower GCL/SCL when it would not only communicate the presence of PPD but also communicate a sense of urgency to take exposure preventing measures. Contact with the different industrial sectors and the labor inspectorate could be pursued to obtain a better understanding of the added value of a more stringent classification for this particular case of PPD.

When an Annex VI dossier for harmonised classification will be taken up it is suggested to also include updating the classification for Acute toxicity. Information on possible carcinogenicity properties of PPD in combination with a coupler or an oxidative agent that may result from a Substance Evaluation is not expected to impact the harmonised classification of PPD as this information concerns combined toxicity of a mixture.

### Restriction

Exposure to PPD leads to very severe alleric skin reactions in workers and consumers. Causes within the scope of the Cosmetics Regulation that involve risks to human health are excluded from restriction under REACH (art. 67.2).

ECHA is currently working on a restriction proposal on CMR and Sensitizing substances in tattoos and permanent make-up. If not already included, it may be considered by ECHA to further explore the possibility to include PPD in the proposal and define the scope of the restriction proposal such that it covers all tattoo-like or temporary tattoo-like applications that are not within the scope of the Cosmetics Directive. This proposal is expected to be submitted for public consultation in the second half of 2017.

Further, there are several other uses for which a restriction could be considered. The Swedisch Competent Authority on REACH is currently developing a restriction on skin sensitizers in textiles. With its harmonized classification as Skin Sensitiser, PPD will fall within the scope currently foreseen for that restriction proposal. To cover possible risks of PPD for consumers, a broad scope including textiles, fur and leather should be considered. The current scope focusses on risks for consumers. Worker risks may not be covered.

Other uses of p-Phenylenediamine are in inks, as a photodeveloper and as a parent compound in vulcanization accelerators and in antioxidants for the rubber industry. These uses could involve risks for workers and consumers. However, only for printers, an indication of a positive association between PPD exposure and the development of a PPD allergy is found in literature. It is therefore uncertain if there is sufficient information available to develop an effective proposal for restriction (e.g. in terms of specific worker conditions or maximum concentration levels in consumer products) and to motivate proportionality of this proposal. Developing a targeted restriction to effectively protect workers may be challenging and required further insight in the different work practices in the sectors involved and in the effectiveness of the protective measures that are already in place. Further study of the actual work practices and possibilities for exposure reduction in the different sectors of use may also be needed when a more broad restriction would be considered covering all uses of possible concern.

Current data on possible causes for the development of a PPD allergy point at a possible risk due to aggregated exposure from different sources. Consequently, restricting the use of PPD in cosmetics via the Cosmetics Regulation, textiles, tattoo’s and possibly also printing inks by focussing on the risk of each use in isolation may not be sufficiently protective. It could therefore be considered to expand the scope of the risk assessment of these targeted restrictions to correct for the possible combined exposure to PPD from uses that are not the subject of the restriction. At the RiME-II 2017 meeting, there seemed no support for restricting the use of PPD without a clear indication for risk. In other words: extrapolating the concern for occupational exposure observed for hairdressers and beautyworkers to other occupations like printers, photodevelopers and workers from the rubber and fuel industry was generally suggested to be difficult and possibly inappropriate in the absence of a clear indication of risk in those other sectors.

Another concern that was recently flagged relates to selftests for sensitization. Recently (March 2017), The Horizon 2020 COST Action TD 1206 “StanDerm” (Development and Implementation of European Standards on Prevention of Occupational Skin Diseases) send a letter to the EU Commission on Internal Market, Industry, Entrepreneurship and SMEs to draw attention to a great concern with regard to self-testing for contact sensitization to hair dyes with the request to communicate this concern to the members of the sub-group “skin allergens” and the Working group on Cosmetic Products. Use of self-tests may constitute a risk for consumers and workers as the concentration of the allergen is typically higher and the conditions of use are typically less well controlled than is the case for allergen-testing by professionals. Concern for risk includes a concern for PPD because of its extreme potency but may equally involve other strong skin sensitizing agents. Further regulation of this type of uses is addressed in the context of the regulation on medicinal products primarily laid down in Directive 2001/83/EC and in Regulation (EC) No 726/2004, and hence is outside the scope of a possible REACH Restriction.

### Authorization

For PPD, the high potency for sensitization and the high occurrence of human health cases described for workers from different sectors and consumers, together with the severity of effects, the delay in onset of effects and the potential for cross sensitization with other substances could suggest that PPD might be of equivalent level of concern to CMR substances. Hence, PPD might meet the criteria for art. 57(f) of the REACH regulation. However, in view of the recent SVHC proposal on HDDA, and even though the profile of human cases for PPD is very different from HDDA, there is a good chance that a proposal for SVHC identification of PPD will not be accepted. On this, RiME-II 2017 suggests that the severity of effects may be contested in the absence of cases leading to hospitalisation. It was nevertheless supported that equivalency of concern compared to 57(a)-(c) should be further assessed when authorisation would be concluded as possible most appropriate risk management measure.

Use of cosmetic products (both by workers and consumers) is outside the scope of Authorisation. The current restriction of PPD under the Cosmetics Regulation and the proposals for restriction under development by ECHA and the Swedish Competent Authority on REACH all focus on reducing risks for consumers. Besides cosmetics, PPD is used by workers under strongly variable conditions. In the absence of information on risks for these uses, authorization of PPD may be an effective instrument to address the concern for this substance in an appropriate manner. Moreover, authorization would leave individual companies a high flexibility in their application for authorization in their detailed description of safe work place specific work practices. Though outside the scope of authorization, candidate listing of PPD might indirectly create an incentive for substitution at the workplace in the production of cosmetics and consequently may lead to a reduction of consumer risks.

The overview of different hair dye ingredients (Table 5) suggests that PPD is not the most potent ingredient that may be brought onto the market, but also that less potent alternatives may be available. Substitution for less hazardous substances may therefore be possible. It should be noted though, that substitution of PPD may not necessarily lead to improved product safety. The technical specifications for use of PPD require an amine moiety or some chemical group that is reactive towards binding peptides. It is therefore questionable that a chemical alternative exists that is not a skin sensitizing agent. And introducing a new sensitizing agent may again lead to new, and potentially larger, health effects in similar or new populations. In addition to these, PPD is said to be most efficient hairdye colorant ingredient to help coloring grey hair. Consequently, substitution of the substance for these type of products on a voluntary basis may be unlikely as it suggests that the possible alternatives may be technically inferior.

Authorization could be considered in addition to the ongoing restriction proposals targeted to protect consumer from EU wide risks of PPD exposure.

## Conclusions on the most appropriate (combination of) risk management options

An overview of the different risk management measures to be considered for PPD in addition to what has already been organized (Table 13) is shown in Table 15.

Table 3 Overview of possible risk management measures for PPD to be considered in addition to already implemented measures

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **OSH** | **Cosmetics Regulation** | **Restriction** | **Authorization** | **SEv** | **CLP** |
| Cosmetics products (overall) |  |  |  |  |  | Skin Sens 1A and Acute tox to improve transparency and communication on hazards and reduce workplace exposure by lowering the generic concentration limit in mixtures |
| Hair dye and eyelashes colouring ingredients |  | Revisiting of safe use workers and consumers; request to IND for further info on safe use |  |  | Further info on carc. Properties depending on the outcome of further actions under the Cosmetics Regulation |
| Black henna tattoos |  | Enforcement of the prohibition | Evaluate scope of ongoing restriction |  |  |
| Dye ingredient in textiles, furs and leather |  |  | Evaluate scope of ongoing restriction |  |  |
| Ink | Enforcement of safe use, BAT, sector agreements |  | Maybe; quantifying risk is challenging | Possible |  |
| Photodeveloping agent | Enforcement of safe use, BAT, sector agreements |  | Maybe; quantifying risk is challenging | Possible |  |
| Vulcantization accelerator and antioxidant in rubber compounds |  |  | Most likely not possible | Possible | Further info on carc. properties |
| Monomer for PPTA polymer |  |  | Most likely not possible | Possible |  |
| Intermediate |  |  | Most likely not possible | Possible |  |
| Antioxidant in fuel -refinery |  |  | Most likely not possible | Possible | Further info on carc. properties |

PPD is widely used in many different sectors ranging from rubber manufacturing to ink to dyes for hair, skin and textiles. PPD is regulated for Cosmetics use and two different proposals for restriction under REACH are under development for use in textiles and use in tattoos and permanent make-up that may impact the safe use of PPD with a focus on risks for consumers. Depending on the eventual scope of these restrictions, the main consumer concerns for PPD may be sufficiently addressed there.

For workers, additional regulatory measures may be considered. Developing an Annex VI dossier to change the harmonized classification from Skin Sens.1 to Skin Sens. 1A would be a first step that may lead to further exposure reducing measures at the workplace. Furthermore, it is suggested to ask the SCCS to revisit their opinion of safe use of PPD in cosmetics by workers, in particular for hairdressers and beauty workers, as cases of sensitization continue to appear. The SCCS opinion should in that case preferably also include further details regarding conditions for safe use such as e.g. labelling of the product used by hairdressers and beauty workers, the supply of gloves with the packaging and instructions for cleaning and disposal of used tools. In addition to these, Authorization may be effective to stimulate substitution and promote the drafting of more detailed workplace safety instruction for non-cosmetic uses, which may be more difficult to achieve and may be more rigidly reached through the route of Restriction. Authorization would impact those uses for which an EU wide risk may not be identifyable but which may add to the overall risk of becoming sensitized to PPD for workers and consumers. This may already be facilitated by identifying PPD as SVHC through Candidate listing.

However, it is highly uncertain wether MSC would be of the opinion that PPD meets the 57(f) criteria for being of Equivalent level of concern. And under the assumption that PPD could meet te criteria of 57(f), it is still debatable that Authorization is an appropriate tool to address concerns for uses for which no clear consumer or worker cases of severe skin sensitization have been identified to date. Primary question here is if those cases are not there and exposure is not sufficiently significant to contribute to a rise in PPD allergy for those people involved, or if cases are not there because these are not identified. It may also be questioned if Authorization is a preferred route, given that substitution of PPD at the workfloor may possibly lead to the introduction of other skin sensitizing substances (also in cosmetic products) giving rise to other, possibly more hazardous effects on workers and consumers. Furthermore, Authorization will not be able to tackle use of PPD in imported articles and will not address the possible important issue of concern from aggregated exposure through multiple sources containing PPD. Consequently, it may be more effective to further assess current underlying reasons of continuing appearance of new worker cases to better understand possible ways to further prevent the development of ever new cases, either in a more voluntary approach with industry and sector organizations, or via a targeted restriction describing best practices for those sectors where EU-wide risks for workers are identified.

In addition to the hazard concern for Skin Sensitization, which is the focus of most current risk management measures, there is a suspicion for carcinogenicity when exposure of PPD coincides with exposure to a coupler or an oxidative agent. If this combined exposure would indeed lead to an increased risk for carcinogenicity, this may impact the risk management measures that are put in place and are under development at this moment. It is therefore concluded that this possible combined effect is further evaluated. Given the mandate of the Cosmetics Regulation, revisiting of the safe use by the SCCS would be a most appropriate first step. Depending on the outcome of this work, further information could be requested through the process of Substance Evaluation. The currently available studies that show negative results on carcinogenicity seem of good quality and it is questionable if new data will provide further insight. Further data generation is therefore suggested to focus on the potential incoherence of available test data. However, as PPD has already been extensively studied by the SCCS, one may argue that providing the SCCS with again a mandate to assess the safe application and use of PPD containing products may be of little added value. In their previous conclusions, the SCCS did point to the possible carcinogenictity of combined uses with oxidative agents on which the industry did not react with further information. When Substance Evaluation will be taken up, it is suggested to add an information request on use and exposure.

To summarize, the following combination of risk management options is suggested:

* CLH for Skin Sens.1A and Acute Aquatic Toxicity;
* SEv to follow-up on the assessment of the SCCS to obtain more info on combined toxicity of PPD with a coupler or oxidative agent, use and exposure;
* Evaluate PPD in the context of the Restriction of Skin Sensitizers in textiles (and maybe fur and leather; Restriction proposal ongoing by SE) and for CMR and Sensitizing substances in tattoo’s and permanent make-up (Restriction proposal ongoing by ECHA);

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1. For more information on the SVHC Roadmap: <http://echa.europa.eu/addressing-chemicals-of-concern/substances-of-potential-concern/svhc-roadmap-to-2020-implementation> [↑](#footnote-ref-1)
2. Please specify the relevant entry. [↑](#footnote-ref-2)
3. MANUAL OF THE WORKING GROUP ON COSMETIC PRODUCTS (SUB-GROUP ON BORDERLINE PRODUCTS) ON THE SCOPE OF APPLICATION OF THE COSMETICS, REGULATION (EC) NO 1223/2009 (ART. 2(1)(A)), VERSION 2.1 (FEBRUARY 2016) [↑](#footnote-ref-3)
4. Permanent hair dyes are formed by mixing three classes of chemicals: primary intermediates, couplers, and an oxidant, usually hydrogen peroxide. When mixed, these chemicals undergo oxidation and coupling reactions to form coloured material inside the hair shaft. The colours are not removed by shampooing. [↑](#footnote-ref-4)