# Patch-test cross-reactivity to a novel, probably non allergenic hair-dye precursor (PPD-derivative F000175918)

Published: 18-10-2011 Last updated: 30-04-2024

Objective: Determination of cross-reactivity to a newly developed PPD-derivative (F000175918) in previously PPD-sensitized patients. Hypothesis:Since PPD-derivative F000175918 is categorized as a moderate sensitizer, based on pre-clinical...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Administration site reactions
Study type	Observational invasive

# Summary

# ID

NL-OMON35429

**Source** ToetsingOnline

**Brief title** Cross-reactivity to PPD-derivative F000175918

# Condition

- Administration site reactions
- Allergic conditions
- Epidermal and dermal conditions

**Synonym** allergic contact dermatitis, contact eczema

### **Research involving**

Human

## **Sponsors and support**

### Primary sponsor: Universitair Medisch Centrum Groningen

1 - Patch-test cross-reactivity to a novel, probably non allergenic hair-dye precurs  $\ldots$  13-05-2025

**Source(s) of monetary or material Support:** samenwerking met Universiteit Trier (Duitsland), Universiteit Trier (Duitsland)

### Intervention

**Keyword:** Allergic contact dermatitis, Cross-reactivity, Epicutaneous patch-testing, Paraphenylenediamine (PPD)

### **Outcome measures**

#### **Primary outcome**

The rate of PPD-sensitized patients that will develop a positive skin reaction

after patch-testing with PPD-derivative F000175918.

#### Secondary outcome

n.a.

# **Study description**

#### **Background summary**

#### INTRODUCTION AND RATIONALE

Para-phenylenediamine (PPD) is an organic molecule which is used in e.g. dark hair dyes, manufactory dyes, dyed leather and rubber.[1] It is categorized in the so-called para-group of aromatic amines. PPD is mainly known because of its use in permanent oxidative hair dyes. These contain colorless low-molecular-weight precursors (e.g. PPD or para-toluenediamine (PTD)) and couplers (e.g. m-aminophenol and resorcinol). Prior to application, the hair dye needs to be mixed with hydrogen peroxide in order to activate the dyeing process.

It is estimated that globally around 70% of the oxidative hair dyes contain PPD.[2] Important properties that make PPD suitable for use in oxidative hair dyes are: a low molecular weight, its penetration ability of the hair shaft and follicle, a high protein binding capacity and its ability to rapidly polymerize in the presence of a coupler and an oxidator.[3]

However PPD is notorious for these features as well; it is a very potent allergen and the global cause of 4-7% of all cases of allergic contact dermatitis.[2] This is one reason why it is included in several standard series

for epicutaneous patch-testing.

The clinical relevance of allergic contact dermatitis to PPD is most apparent in individuals exposed to oxidative hair dye, namely consumers and hairdressers. Once sensitization has occurred, re-exposure to a PPD containing compound leads to a dermatitis which, depending on the strength of the T-cell mediated immune response (type IV), varies in severity. Symptoms may include redness, swelling, itching, blistering and/or scaling of the scalp, neck, ears, face and (in hairdressers) hands.[4]

Despite this, the use of oxidative hair dyes, and thus the prevalence of PPD sensitization, is growing worldwide. In the past hair dyeing was mainly a proceeding to camouflage grey hair, today it's a certain part of fashion and commerce. Nowadays 60% of Dutch women dye their hair. In men over 40 years of age this is 10%. Also consumers are starting at a younger age with dyeing their hair, and they continue this for a longer period. The most commonly used hair care products in the Netherlands are the permanent oxidative hair dyes, with a market share of 65%.[5]

Sensitization and type IV reactions to PPD and other molecules from the para-group can also be caused by a cross-reaction between these molecules.[6,7] For example, a previously PPD-sensitized individual can develop an allergic contact dermatitis to PTD without ever been in contact with that molecule.

The immunological causes for cross-reactivity are not fully explained yet. One possible theory is that contact allergens consist of so called pro-haptenes, which are metabolized in the skin to common metabolites, namely haptenes. Bound to a protein these then function as allergenes and may stimulate the proliferation of T-cells.[8] Why in case of exposure to PPD some people will develop sensitization, whereas others not, is still subject of research. One possibility is that differences in enzymatic breakdown of PPD (by N-acetyltransferase 1 in keratinocytes) exist due to interindividual genetic variation and/or environmetal factors.[9] At present the problem of cross-reactivity is, in assessing the toxicological profile of newly developed molecules, no routine yet.

In our study a newly developed molecule, which is planned to substitute for PPD, will be examined for possible cross-reactivity in PPD-sensitized individuals. PPD-derivative F000175918 has been subjected to extensive pre-clinical studies of acute and repeated dose toxicity, genotoxicity, reproductive toxicity, irritation, sensitization and skin penetration.[10] The safety evaluation for PPD-derivative F000175918 was conducted in accordance with the "Notes of Guidance for Testing of Cosmetic Ingredients and Their Safety Evaluation by the SCCP", released by the European Commission in 2006.

Summary of this safety evaluation:

•The maximum on-skin concentration of PPD-derivative F000175918 is 3%.

•The use of PPD-derivative F000175918 in the salon testing phase with more than 100 volunteers has been successfully completed (data not published).

•At the maximum on-skin concentration of 3%, PPD-derivative F000175918 is not considered to cause eye irritation, skin irritation or skin corrosion.

•From a local lymph node assay (LLNA) PPD-derivative F000175918 is categorized as a moderate skin sensitizer, with an EC3 value of 7.11%. As a comparison, PPD is a strong sensitizer with an EC3 value of 0.1%. Thus PPD-derivative F000175918 is very unlikely to give sensitization and it also seems to have very low potency to induce cross-reactivity.

•PPD-derivative F000175918 did not show teratogenic potential up to the highest dose.

•PPD-derivative F000175918 has no genotoxic potential under in vivo conditions. Therefore, PPD-derivative F000175918 is considered not to give any risk to humans with regard to mutagenicity.

A previously performed study of PPD-derivative F000175918, with patch-testing 16 PPD-sensitized subjects for 48 hours with 1% of the substance in petrolatum, gave 1 positive (+++) reaction. (Toxicology Department, University of Trier, Germany, data not published)

In conclusion, with the increasing use of oxidative hair dyes worldwide and the concomitant increase in PPD-allergy, the development and industrial introduction of a moderately allergenic substitute for the strongly allergenic PPD is very desirable.

### **Study objective**

Objective:

Determination of cross-reactivity to a newly developed PPD-derivative (F000175918) in previously PPD-sensitized patients.

Hypothesis:

Since PPD-derivative F000175918 is categorized as a moderate sensitizer, based on pre-clinical toxicological studies and given the result of the pilot study with regular patch-testing, our hypothesis is that no subjects, yet at the most one subject, will react positive at patch-testing in our study design.

### Study design

Observational study with the use of epicutaneous patch-testing and without the use of a medicinal product or other invasive measurements.

#### Intervention

Epicutaneous patch-testing with PPD-derivative F000175918 in a basic compound and with the basic compound alone (control testing).

### Study burden and risks

No serious side effects can be expected during and after patch-testing. A possible cross-reaction to the PPD-derivative or an irritant reaction to the test-chambers are issues that have been discussed in this form and in the research protocol.

The time burden on subjects is minimal and also discussed before.

Subjects do not directly benefit from this study.

# Contacts

#### Public

Universitair Medisch Centrum Groningen

Hanzeplein 1 9700 RB Groningen NL **Scientific** Universitair Medisch Centrum Groningen

Hanzeplein 1 9700 RB Groningen NL

# **Trial sites**

## **Listed location countries**

Netherlands

5 - Patch-test cross-reactivity to a novel, probably non allergenic hair-dye precurs ... 13-05-2025

# **Eligibility criteria**

Age Adults (18-64 years) Elderly (65 years and older)

### **Inclusion criteria**

-History of allergic contact dermatitis to PPD and a positive patch-test to PPD -Adulthood (>=18 years) -Legal competence

## **Exclusion criteria**

-Active skin disease at volar side of forearms
-Legal incompetence
-Pregnancy
-Use of immunosuppressive drugs

# Study design

### Design

Study type: Observational invasive		
Masking:	Open (masking not used)	
Control:	Uncontrolled	
Primary purpose:	Prevention	

### Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	24-11-2011
Enrollment:	38
Туре:	Actual

6 - Patch-test cross-reactivity to a novel, probably non allergenic hair-dye precurs ... 13-05-2025

# **Ethics review**

Approved WMO	
Date:	18-10-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

# **Study registrations**

# Followed up by the following (possibly more current) registration

No registrations found.

# Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

**Register** CCMO **ID** NL37949.042.11