Ministry of Environment and Gender Equality
Environmental Protection Agency

Survey and risk assessment of chemical substances in spectacle frames

Survey of chemical substances in consumer products No. 201

March 2025

Title: Survey and risk assessment of chemical substances in spectacle frames

Purpose:
The objective of this project was to investigate the materials and potentially harmful substances that might be found in plastic spectacle frames, which can lead to allergic reactions like swelling and eczema. Through chemical analyses and risk assessments, the study also aimed to determine whether specific substances in plastic spectacle frames, across various price points, could pose a risk to children or adult users.

Prepared by: DHI A/S og FORCE Technology

Prepared for: The Danish Environmental Agency

Financed by: The Danish Environmental Agency

Delivery Date of the Report: 6. februar 2025

Publisher: The Danish Environmental Protection Agency

Editorial office:
Sara Højriis (DHI A/S)
Poul Bo Larsen (DHI A/S)
Ingelise Dige Semark (DHI A/S)
Dorthe Nørgaard Andersen (DHI A/S)
Pia Brunn Poulsen (FORCE Technology)
Rikke Munch Gelardi (FORCE Technology)
Susann Geschke (FORCE Technology)

ISBN: 978-87-7038-725-5

Content

Preface		**5**
Summary		**6**
Glossary		**11**
1.	**Introduction**	**13**
1.1	Background	13
1.2	Purpose	13
1.3	Scope	13
1.4	Project phases	14
2.	**Legislation**	**15**
2.1	REACH	15
2.2	Medical devices	15
2.3	CE marking	16
2.4	Checking compliance with applicable legislation	17
3.	**Survey**	**18**
3.1	The Danish market for spectacle frames	19
3.2	Identification of material types for spectacle frames	19
3.2.1	Danish opticians' range of spectacles	19
3.2.2	Other spectacle retailers and their range of spectacles	22
3.2.3	Recycled plastic	22
3.2.4	Identified material types	23
3.3	Identification of problematic substances in spectacle frames	23
3.3.1	DHI's Plastic Material Database	24
3.3.2	Literature search	27
3.3.3	Contact with the National Allergy Research Centre	34
3.3.4	Summary, identification of problematic substances in spectacle frames	35
3.4	Selection and purchase of spectacle frames for analysis	40
3.5	Exposure scenarios	41
4.	**Screening analyses**	**43**
4.1	Analytical issues	43
4.2	FT-IR for identification of the material in the spectacles	44
4.2.1	Results of FT-IR analyses	44
4.3	Sample preparation for GC-MS and TLC	45
4.4	TLC for identifying certain dyes	46
4.5	GC-MS Screening for Organic Substances	49
4.6	Prioritisation of substances for migration analyses	57
4.6.1	Overall hazard assessment and prioritisation of the most important substances from the GC-MS screening	62
4.6.2	Conclusion concerning prioritisation of substances for migration analyses	65
5.	**Migration analyses**	**66**

5.1	Choice of migration fluid	66
5.2	Method of analysis	67
5.2.1	Sample preparation	67
5.2.2	Performance of migration tests and quality data of the analysis method	68
5.3	Results of the migration analyses	68
5.4	Discussion of the analysis results	70
5.4.1	Discussion of coloured migration fluids	71
6.	**Hazard assessment**	**72**
6.1	Drometrizole (CAS 2440-22-4)	73
6.1.1	General data	73
Chemical Formula		73
6.1.2	Toxicological data	74
6.2	4-tert-amylphenol (CAS 80-46-6)	76
6.2.1	General data	76
Chemical Formula		76
6.2.2	Toxicological data	76
6.3	*o*-Acetyltriethyl citrate (CAS 77-89-4)	79
6.3.1	General data	79
Chemical Formula		79
6.3.2	Toxicological data	80
6.4	Triethyl citrate (CAS 77-93-0)	82
6.4.1	General data	82
Chemical Formula		82
6.4.2	Toxicological data	82
6.5	Summary	84
7.	**Risk assessment**	**86**
7.1	Methodology	86
7.2	Exposure assessment	86
7.3	Risk assessment	88
7.3.1	Risk assessment of the individual frames	88
7.4	Uncertainties in the assessments	92
7.5	Summary and discussion	94
References		**96**

Preface

Survey and risk assessment of chemical substances in spectacle frames

In this project, the occurrence of problematic substances in spectacle frames that are available to the Danish consumer has been investigated. Dyes and sensitising substances have been in focus as there has been an increasing incidence of allergy cases when using plastic frames, caused by dyes in the plastic.

The report presents the results of the survey, the chemical analyses and the hazard and risk assessment.

The project was carried out by DHI A/S with FORCE Technology as a subcontractor for the chemical analyses. In addition, the industry and the National Allergy Research Centre have contributed important knowledge to the project.

The project participants were:

Sara Højriis, DHI A/S
Poul Bo Larsen, DHI A/S
Ingelise Dige Semark, DHI A/S
Dorthe Nørgaard Andersen, DHI A/S

Pia Brunn Poulsen, FORCE Technology
Rikke Munch Gelardi, FORCE Technology
Susann Geschke, FORCE Technology

The project was monitored by the following employees from the Danish Environmental Protection Agency (Danish EPA):

Maria Thestrup Jensen
Grete Lottrup Lotus

The project was funded by the Danish EPA

The project was carried out between November 2023 and November 2024.

Summary

Objective
The Danish Environmental Protection Agency regularly receives enquiries from citizens who experience discomfort such as swelling and eczema in connection with the use of plastic spectacles, and the National Allergy Research Centre also reports an increase in patients with facial eczema after skin contact with plastic spectacles and temples.

This project aims to map the materials used in spectacle frames and the substances of concern that may be present in spectacle frames, with a particular focus on plastic frames due to their content of dyes and other additives. Using chemical analysis and knowledge of the harmful effects of the substances, the content of problematic chemical substances in a range of frames was identified and risk assessment for consumers was made for selected frames.

Mapping and knowledge gathering
The survey gathered knowledge about the materials used in spectacle frames through websites or direct contact with a number of large optician chains, manufacturers and other spectacle retailers such as supermarkets and DIY stores. The impression from this knowledge gathering is, that knowledge regarding frame materials used and their chemical composition is generally very limited: In many cases the materials were simply described as plastic or synthetic, however, some market players were able to further differentiate their products into different plastic categories such as acetate, cellulose propionate, nylon, polycarbonate or polyetherimide. In general, there was a lack of knowledge about the content of problematic substances or specific ingredients such as UV filters, antioxidants, plasticisers and dyes. In the case of metal frames, there was an awareness of the presence of nickel, which is a well-known skin sensitiser.

One of the larger optician chains stated that they had up to 40 different suppliers, each of which supplied up to 20 different brands of spectacle frames, which added to the overall picture of a very wide differentiated market for spectacle frames.

Substances of concern
Based on information gathered from the National Allergy Research Centre and further searches in the literature, a large number of substances of concern have been identified that may pose a risk to consumers when used in spectacle frames. TABLE 17 in this report lists 17 dyes considered as skin sensitisers, while TABLE 18 lists 45 other ingredients in plastic, most of which are classified as either carcinogenic, mutagenic, toxic to reproduction or as skin sensitisers.

Screening analyses
In agreement with the Danish Environmental Protection Agency, 19 frames/frame materials made of plastic or synthetic materials were purchased/collected from online shops or from manufacturers. The frames were purchased to represent the current market in terms of material (type of plastic), colour, price and design. However, only plastic or rubber frames or temple tips (rubber tubes attached to metal temples) were purchased and analysed. Four of the 19 frames were children's frames. For the majority of the 19 frames, FT-IR analysis was performed to identify the material of the frames. Most of the frames were made of cellulose acetate or cellulose propionate, but frames made of nylon, polycarbonate and other plastic blends were also identified.

Thin layer chromatography (TLC) was used to test for the presence of selected allergenic dyes in purchased frames. In general, the method was found not to be optimal for the detection of dyes as some of the dyes were difficult to separate and therefore difficult to identify. However, the screening did detect Solvent Orange 60 in several frames, as well as possible identification of Solvent Yellow 14, Solvent Red 179, Disperse Orange 3, CI Solvent Yellow 1 and Disperse Red 1 in some frames. The result of the TLC screening indicated that 11 out of 19 frames contained one or more allergenic dyes that have previously caused allergic reactions in eyeglass wearers.

Finally, a GC-MS screening was performed in extracts from the 19 spectacles frames to semi-quantitatively determine the content of volatile/semi-volatile organic compounds. This GC-MS screening identified several phthalates in a wide range of the frames analysed. The phthalate DEP was identified in several of the frames/materials tested and in a handful of frames the levels may have been 10% or more. Many other organic substances were also identified in the extracts, but only a few of these substances had an EU harmonised classification as either CMR or as skin sensitiser. However, the levels of these substances in the frames were probably very low.

In the further prioritisation of substances found in the screening analyses for further migration analysis and risk assessment, the following criteria were used to identify substances:

- Number of frames in which the substance was found
- Estimated high content in the screening analysis, so that the substance is expected to be identifiable in a migration fluid
- Critical effect of the substance, with emphasis on skin sensitisation effects

It was decided not to focus on dyes for the migration analyses as the allergy risk associated with their use is relatively well known, e.g. the National Allergy Research Centre has already reported of series of patients having has allergic reactions to specific dyes.

Based on the above criteria, 13 organic substances from the screening analysis were selected for further evaluation for critical effects, and based on an overall evaluation of these substances, the following four substances were selected and purchased as reference substances for the migration analyses:

- Drometrizole (CAS 2440-22-4)
- 4-tert-amylphenol (CAS 80-46-6)
- *o*-acetyl triethyl citrate (CAS 77-88-9)
- Triethyl citrate (CAS 77-93-0)

Migration analyses
The six frames in which the four selected substances were identified in the highest concentration by the GC-MS screening were selected for migration analyses. The result of the migration analysis was that the four substances drometrizole, 4-tert-amylphenol, *o*-acetyl triethyl citrate and triethyl citrate were identified in the migration fluid of five, three, six and six of the six frames analysed. This means that all four substances migrate out of the frames and can potentially cause skin sensitisation and allergic reactions. The substances *o*-acetyl triethyl citrate and triethyl citrate migrated the most from the frames, but by far the most migration was observed for *o*-acetyl triethyl citrate in frames 11 and 13.

Hazard assessment
The hazard assessment of the four substances was carried out by collecting toxicological data from the substances' REACH registration dossiers combined with data from international expert assessments. In one case it was also necessary to obtain original toxicological literature on the substances.

Based on these data, critical effects related to local skin exposure (irritation and sensitisation) and critical systemic effects (i.e. effects on internal organs that may occur after the substance has been absorbed and distributed in the body) were assessed.

On the basis of these data, tolerable exposure levels (DNELs) were calculated for the substances, expressed partly as µg/cm2 for dermal load on the skin (for the risk assessment for local effects) and partly as µg/kg bw/day (for the risk assessment for systemic effects).

Exposure assessment
Local dermal surface exposure
The analytical results of the migration test are expressed as the amount of substance released per cm^2 from the spectacle frames after 72 hours of migration. The values are used as a worst-case estimate to assess the amount of skin exposed per cm^2 of skin per day by multiplying the measured migration value by a factor of 18 hours/72 hours = 0.25, assuming that the spectacles are worn up to 18 hours per day. The calculation assumes that the spectacles release the same amount of substance per cm^2 over time as measured in the migration analyses.

Total exposure from contact with the spectacle frames
The total exposure from a spectacle frame, expressed in µg/kg bw/day, can be calculated from the daily release of the substance per cm^2 of frame multiplied by the area of the frame in contact with the user's skin and divided by body weight:

Total exposure (µg/kg bw/day) = total contact area (cm^2) x daily release per cm^2 (µg/cm^2/day)/ 60 kg

In the above, a body weight of 60 kg has been used for adult users and a body weight of 35 kg for children.

Risk assessment
In the actual risk assessment, the exposure levels are compared with the tolerable exposure levels for the substances (i.e. the DNELs). This is done by calculating the risk characterisation ratio (RCR):
RCR = Exposure value / DNEL value
In cases where the exposure exceeds the DNEL, the RCR will be greater than 1, indicating that there is a potential risk associated with the exposure.
In cases where the exposure is below the DNEL, the RCR will be less than 1, indicating that the exposure poses no risk.
In borderline cases, where the RCR is just above or just below 1, it will be necessary to further analyse the data in terms of uncertainties in the calculations and assumptions made in the exposure assessment and in setting of the DNEL.

A risk assessment table with RCR values for local effects, and RCR values for systemic effects has been prepared for each of the frames. Only for frames nos. 11 and 13 RCR values greater than 1 were obtained, while the RCR values for the other frames were significantly less than 1.

The table below summarises the results of the risk assessments of the six frames, based partly on the quantitative analyses of the migration test and partly on the screening analyses of the dye content in the TLC extracts:

	Risk assessment of migration of 4-tert-amylphenol *o*-acetyl triethyl citrate triethyl citrate drometrizole			Risk assessment of qualitative findings in TLC extracts of Solvent Orange 60; Solvent Red 179; Solvent Yellow 1; Disperse Orange 3; Disperse Red 1
	Local effects	**Systemic effects**	**Critical substance**	**Dye in TLC extracts Potential risk**
Spectacle frame 4	No risk	No risk	-	Faint pink migration fluid. No findings of the above mentioned dyes.
Spectacle frame 11	Potential risk, sensitisation	Potential risk*	*o*-acetyl triethyl citrate	Dark blue migration fluid Solvent Orange 60 and Solvent Red 179. Skin allergy has been observed with both when used in spectacle frames. Potential risk, sensitisation.
Spectacle frame 13	Potential risk, sensitisation	Potential risk*	*o*-acetyl triethyl citrate (triethyl citrate)	Colourless migration fluid. No detection of the above mentioned dyes.
Spectacle frame 16	No risk	No risk	-	Strong brown/orange migration fluid. Solvent Orange 60 for which skin allergy has been observed when used in spectacle frames. Potential risk, sensitisation.
Spectacle frame 17	No risk	No risk	-	Faint pink migration fluid. CI Solvent Yellow 1. The substance has an EU harmonised classification with Carc. 1B H350. Unknown risk.
Spectacle frame 18	No risk	No risk	-	Red migration fluid. Disperse Orange 3 and Disperse Red 1. Skin allergy has been observed for both substances when used in spectacle frames. Potential risk, sensitisation.

* Indicates that the calculated risk has a high degree of uncertainty

It should be noted that the dyes listed in the table have only been identified in extracts from the spectacles in the TLC screenings carried out and therefore no attempt has been made to identify them in the migration fluid. The fact that the migration fluid is coloured may be due to one of the dyes identified in the TLC screening, but it may also be due to other dyes as the migration fluid was not TLC screened.

As can be seen, it is the substance *o*-acetyl triethyl citrate (used as a plasticizer) that poses a risk of skin sensitisation for the two spectacle frames nos. 11 and 13. This is mainly due to the high local dermal exposure of 965 µg/cm^2 and 4300 µg/cm^2, resulting in RCR values of 13 and 58 respectively. For the systemic effects, RCR values were above 1 for this substance in both spectacle frames, but here the uncertainty in the exposure estimates over time, and also in the determination of the DNEL-value is considered too high to draw a more reliable conclusion.

Overall, the report has identified a number of problematic - mainly skin sensitising - substances used in spectacle frames and demonstrated that these can migrate out of the frames and pose a skin sensitisation risk to the user. It should be noted that o-acetyl triethyl citrate has not previously been listed as a critical substance in spectacle frames.

Further, it is to be noted that there is very limited awareness and knowledge of the use of problematic additives among opticians, manufacturers and suppliers of spectacle frames.

Glossary

Authorisation List	List of chemical substances included in Annex XIV of REACH, all of which are subject to approval. The chemical substances on the authorisation list have inherent properties, usage quantities and/or distributions that require authorisation before use.
Candidate List	The EU Candidate List of Substances of Very High Concern (SVHC) is a list of chemical substances that are considered to be of very high concern for human health or the environment. Falls under REACH. The list shows consumers and companies which chemicals are candidates for the authorisation list.
CLP Regulation	(EU Regulation No. 1272 of 2008) is the applicable EU legal regulation for the classification and labelling of chemical substances and mixtures. CLP stands for "Classification, Labelling and Packaging"; classification, labelling and packaging.
Contact allergy	Contact allergy is also called skin allergy, the cell-mediated allergy, type IV allergy or the delayed allergic response. Contact allergy occurs when there is skin contact with chemical substances that can cause allergies, such as perfumes, metals, dyes and preservatives.
Depigmentation	Total or partial loss of the skin's normal pigmentation. Temporary reduced pigmentation may occur in eczema.
Eczema	Also referred to as dermatitis, is inflammation of the skin. Symptoms are redness, itching, blistering, peeling, swelling and cracks in the skin.
List of Restrictions	See explanation under 'Restriction list'.
Masterbatch	A polymer containing a large concentration of pigment, which is added to the uncoloured polymer in a certain ratio to achieve a specific shade of colour.
Patch test	During a patch test, one is exposed to small amounts of the allergenic substances that are suspected to be the cause of the eczema. By using the patch test, it is possible to demonstrate whether the patient has an allergy to specific chemical substances.
REACH	An EU regulation ((EC) No. 1907/2006) that regulates chemical substances that are placed on the market in the EU. As the REACH Regulation is fully harmonised in the EU, the Regulation is directly applicable in Denmark.
Restricted list	Restriction list under REACH (Annex XVII). Also known as 'List of restrictions'. These chemical substances have limitations on their use, placing on the market and manufacturing in the EU.

SVHC	"Substance of Very High Concern". Substances that can have serious effects on humans and/or the environment. Primarily substances that are carcinogenic, mutagenic or toxic to reproduction, as well as substances with persistent and bioaccumulative properties. They can also be, for example, endocrine disruptors. SVHCs are chemical substances that are officially identified in the EU as candidates for inclusion on the authorisation list due to the above serious properties. SVHC substances appear on the EU's Candidate List.
Temple tip	The piece on the temple (arm) of the spectacle frame that sits behind the ear. Most often plastic or rubber on metal spectacle frames.

1. Introduction

The Danish Environmental Protection Agency has received regular enquiries from citizens who experience discomfort in the form of eczema and swelling when wearing spectacles and reports an increasing trend of patients referred to the National Allergy Research Centre with facial eczema after wearing spectacles. Therefore, in 2023-2024, the Danish Environmental Protection Agency initiated a project with a survey and risk assessment of chemical substances in spectacle frames, which are available to Danish consumers.

1.1 Background

Spectacles are intended to assist consumers with impaired vision (both farsightedness and near-sightedness). According to the Danish Eye Association for Protection of Sight, about 60% of the Danish population uses spectacles. The association estimates that approx. 20% of children under the age of 12 use spectacles[1]. The percentage increases with age, which is why the percentage for consumers over the age of 40 is up to 80% of the population and as much as 92% for people over 60[2]. In addition to the part of the population that wears spectacles due to impaired vision, spectacles have also begun to be used as fashionable accessories.

The Danish EPA regularly receives enquiries from citizens who experience discomfort such as swelling and eczema associated with the use of spectacles, and the Danish EPA reports that the National Allergy Research Centre has recently seen an increase in patients with facial eczema after skin contact with plastic spectacles/temples. To identify which allergens could specifically be the cause of this trend, the National Allergy Research Centre conducted a study to determine the allergens in plastic frames. The study showed that just over a third (7/19) of the included patients reacted to scrapings from the spectacle frames and dyes (Ahrensbøll-Friis et al. 2021)

1.2 Purpose

The background of this project is the combination of the large percentage of Danish consumers who wear spectacles and the increasing tendency for facial eczema when in contact with spectacles. The project surveyed which materials are used for spectacle frames and which problematic substances can potentially be present in spectacle frames. The content of problematic chemical substances has been identified and the risk to consumers from the use of spectacle frames has been determined with the help of analyses and risk assessments.

1.3 Scope

The Danish EPA assesses that contact allergy caused by metal frames is typically caused by nickel content (which is extensively regulated), and the focus of this report is therefore on frames of other types of material (assessed to be primarily plastic) and potentially problematic ingredients in these. However, metallic spectacle materials were included in the survey of spectacle materials on the Danish market and were included in the identification of problematic substances in the literature search.

The project includes spectacle frames for adults and children with farsightedness and near-sightedness. Sunglasses, safety spectacles or spectacles that are used exclusively as fashion accessories are not included.

[1] More and more Danish children are becoming nearsighted | The Danish Eye Association (ojenforeningen.dk)

[2] https://www.louisnielsen.dk/stillede-sporgsmal/hvor-mange-bruger-briller

1.4 Project phases

The project consisted of four phases:

Phase 1: Survey on spectacles frames (November 2023 to January 2024)
Phase 2: Analyses; Screening and migration analyses (February to June 2024)
Phase 3: Hazard Assessment (April 2024)
Phase 4: Exposure and risk assessment (August 2024)

The report contains a chapter for each of the four phases, which describes the method and results for the sub-phase. Finally, the report contains a discussion of all the results of the phases, as well as a conclusion of whether spectacle frames can pose a risk for Danish consumers.

2. Legislation

This chapter briefly describes the legislation that applies to spectacle frames for farsightedness and near-sightedness.

2.1 REACH

The REACH Regulation ((EC) No. 1907/2006) is an EU regulation that regulates chemical substances that are placed on the market in the EU, e.g. in articles. As the REACH Regulation is fully harmonised in the EU, the Regulation is directly applicable in Denmark.

The regulation obliges companies in the EU that produce, import, distribute or use chemical substances or mixtures to register the import and/or manufacture of the substances. The manufacture, placing on the market and use of substances, mixtures and articles are regulated, inter alia, through restrictions of use (REACH, Annex XVII) and an authorisation scheme (REACH, Annex XIV).

The REACH Regulation is relevant for spectacle frames, as spectacle frames belong to the category of articles. The restrictions of use in REACH, Annex XVII are of particular relevance. This Annex is a list of conditions under which substances or groups of substances may or may not be used, placed on the market and/or manufactured. Restrictions on the use of chemical substances in different materials and products are considered to be relevant for spectacle frames.

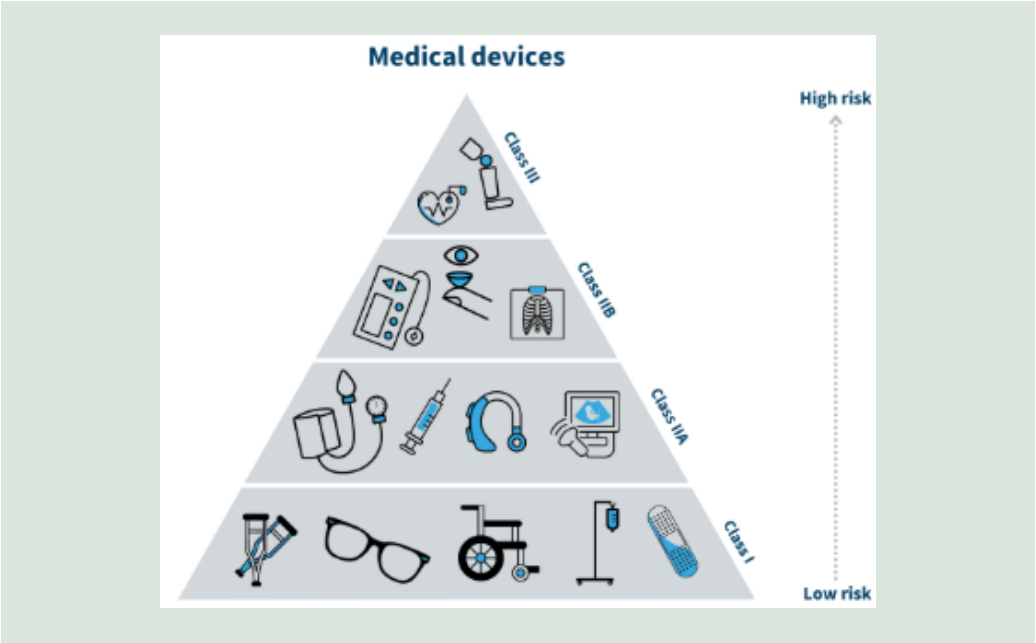
2.2 Medical devices

Medical devices are products that are used to diagnose, prevent, alleviate, or treat diseases, disabilities, or injuries. It is stated in the current guidelines "Guidelines for start-up manufacturers of medical devices" (VEJ no. 9376 of 21/05/2021) that mass-produced spectacle frames (and spectacle lenses) are medical devices.

Medical devices are divided into the risk classes I, IIA, IIB, III, which are used, among other things, to indicate the safety and performance requirements that must be met before the product can be marketed in EU. Class I is associated with the lowest risk, while Class III is associated with the highest risk. Spectacles are a "Medical device"[3] in risk class I and thus associated with the lowest risk.

Medical devices are regulated by two EU regulations, the overall purpose of which is to ensure patient safety. The two regulations in this area are, respectively, an EU regulation on medical devices and an EU regulation on medical devices for *in vitro*-diagnostic uses (IVD). As spectacle frames do not belong to the category of IVD medical devices, this Regulation is not applicable to spectacle frames.

[3] Guidance for distributors and importers of medical devices (laegemiddelstyrelsen.dk)



FIGUR 1. Examples of medical devices and their risk class, https://laegemiddelstyrelsen.dk/en/devices/

2.3 CE marking

Spectacle frames must be CE marked in order to be placed on the European market. A CE marking shows that the product/device complies with the applicable EU legislation both with regard to the Medical Device Regulation and REACH. In the case of medical devices in a risk class higher than class I, the assessment of whether the product can be CE marked must be carried out by a notified body. As spectacle frames belong to class I they and can be placed on the market in EU without involvement of a notified body.

Medical devices must meet the general safety, performance and labelling requirements of the Medical Devices Regulation. This means that the device must be safe to use and capable of performing the intended purpose stated by the manufacturer. The device must be manufactured and designed to be capable of performing the intended purpose stated by the manufacturer. In order to demonstrate that the device meets the general safety and performance requirements, the manufacturer must therefore have a risk management system, a quality management system and conduct a clinical evaluation. Based on the results of the risk management system, quality management system and clinical evaluation, the manufacturer must prepare technical documentation to demonstrate that the product has the characteristics stated by the manufacturer. Once the general safety and performance requirements have been met and the manufacturer's technical documentation has been prepared, the manufacturer must date, sign and keep a declaration of conformity stating that the product complies with the requirements of the Regulation.

In order to obtain CE marking, the supplier to the EU market must therefore meet the assessment and safety requirements for medical devices specified in the EN ISO 10993-1:2020 standard: "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process" as well as the other more detailed sub-standards in the ISO-10993 series, where in particular EN ISO 10093-18:2020 regarding chemical characterization and EN EN ISO-10093-17:2023 regarding the risk assessment of medical device constituents are relevant for the safety assessment of the medical device.

2.4 Checking compliance with applicable legislation

Verification of compliance with REACH is within the remit of the Danish Environmental Protection Agency's Chemicals Inspectorate. Control of the legislation for medical devices is within the remit of the Danish Medicines Agency. The Danish Medicines Agency does not approve medical devices, but they supervise Danish manufacturers, importers, distributors and authorised representatives in the field of medical devices. The Danish Medicines Agency reacts when it becomes aware of errors, failures or deficiencies in medical devices. This is done, among other things, on the basis of reports of incidents involving medical devices that are received from e.g. manufacturers, healthcare professionals or citizens.

3. Survey

The purpose of the survey was to gather knowledge about the types of materials used for spectacle frames for adults and children, and which harmful substances can be found in the different types of materials.

In order to shed light on this, the survey consisted of the following sub-activities:
- Identification of material types
- Identification of substances of concern
- Initial hazard assessment of identified substances of concern
- Selection of spectacle frames for analyses

The survey thus primarily consisted of the collection of relevant information. The following methods were used to collect information:
- Internet searches to identify webshops selling spectacle frames
- Contact with the industry, e.g. opticians, opticians' chains and manufacturers
- Contact with the National Allergy Research Centre
- Literature search

Initially, several of the major opticians' websites have been visited: Synoptik, Thiele, Louis Nielsen and Profil Optik. The purpose of this was to identify the different materials used for spectacle frames on the Danish market, and to identify suppliers and/or manufacturers. At the same time, a literature search was conducted for problematic substances previously identified in spectacle frames.

Contact with the industry
The industry was contacted to gather knowledge that could supplement the literature on problematic substances in spectacle materials. They were also asked about sales statistics for the various eyewear materials, as well as where the production of spectacle frames occurs (Denmark, EU or non-EU). A large number of opticians, suppliers, manufacturers and a single polymer distributor were contacted.

In general, opticians and manufacturers stated that they were not aware of problematic substances in spectacle frames, e.g. allergenic substances or problematic plasticisers in plastic spectacle frames. One manufacturer reported that they were aware of the problem of allergenic substances in spectacle frames, as spectacle frames that do not cause contact allergy are sometimes requested. In such cases, the manufacturer was unable to comply with the customers’ wishes, as the manufacturer itself was not aware of specific problematic ingredients in the spectacle material.

The polymer distributor stated that it is their customer (the spectacles manufacturer) who sets the criteria for the production of masterbatches (a polymer containing a high concentration of pigment which is added to the non-coloured polymer in a certain ratio to achieve a certain shade of colour). This means that a multitude of different masterbatches can be expected with specific contents of chemical substances, including dyes. It was stated that there is a great deal of confidentiality about which masterbatches are specifically used and which ingredients they consist of. The problem regarding information about ingredients in spectacles is confirmed by the National Allergy Research Centre, which reports that it is impossible to obtain information about ingredients in spectacles.

The industry could not be helpful with information about specific ingredients, but there were several who gave an estimate of the material distribution for sold spectacles (included in TABLE 4).

3.1 The Danish market for spectacle frames

In Denmark, there are a multitude of opticians who offer eye tests and spectacles. In 2022, the market for the sale of spectacles had sales of DKK 4316 million[4]. The largest opticians[5] include Synoptik, Thiele, Louis Nielsen and Profil Optik. Profil Optik, (which is the Danish brand under Synsam) stated that they have a market share of 22% of the market with their 116 shops[6]. Other major players in the Danish market include Synoptik, Thiele and NytSyn. As an example of the number of spectacles sold, Louis Nielsen reported that it sells more than 400,000 spectacles a year in its 80 shops[7].

Customers can choose their own spectacle frames in the many physical and internet-based shops. The spectacle frames are delivered to the optician's shops by companies/suppliers who supply spectacle frames of many different brands from different manufacturers. One of the larger optician chains states that they have up to 40 different suppliers, each of which supplies up to 20 different brands. Some opticians/opticians' chains also produce their own spectacle frames. The market for the sale of spectacle frames is thus characterised by many players and many steps from manufacturer to consumer.

3.2 Identification of material types for spectacle frames

The identification of different types of material used for spectacle frames was made by an internet search and a few shop visits.

Spectacle frames typically have contact with the wearer's skin on and behind the ears, on the side of the head and, in the case of spectacles without nose pads, also with the skin on the nose. The nose pads are typically made of silicone. In this project, it has been chosen to focus exclusively on the ingredients in the spectacle frames themselves, which is why the literature search does not include any information about the nose pads.

When identifying material types, the starting point has been the following:

- Danish opticians (the largest opticians in Denmark), including Synoptik, Thiele, Louis Nielsen and Profil Optik
- The retail trade, including Matas, pharmacies, supermarkets and discount department shops, e.g. Harald Nyborg.

3.2.1 Danish opticians' range of spectacles

Below is an overview of the different types of material identified on the four websites: Synoptik, Thiele, Louis Nielsen and Profil Optik.

Synoptik

On Synoptik's website (synoptik.dk/briller), there were 1040 different spectacles in their range when the search was made. Of the 1040 spectacle frames, 961 were frames for adults and 79 frames for children.

For the 961 different frames for adults, the following material types were identified on the website:

- Metal (344 types)

[4] https://estatistik.dk/branche/optikere/477810

[5] https://estatistik.dk/branche/optikere/477810

[6] Danmark – Synsam Group

[7] Louis Nielsen is part of Specsavers | Louis Nielsen

- Plastic (296 types)
- Acetate (247 types)
- Titanium (74 types)

For the 79 frames for children, the following material types were identified:
- Metal (33 types)
- Plastic (24 types)
- Acetate (20 types)
- Titanium (1 types)

The frames are from approx. 50 different brands and are in the price range: DKK 198 - 4298. The cheapest brand is "Seen", that has 72 different types available. Of these, 41 are plastic, 29 metal, and 2 acetates. The most expensive spectacles are in the price range: DKK 2970 - 4298, with 89 frames available on the website. These frames are from several different brands: Silhouette, Bvlgari, Gucci, Tom Ford, Saint Laurent, Starck Biotech, Tiffany & Co., Chloe and Giorgio Armani. Of these, 33 are metal, 29 plastic, 19 acetate and 8 titanium.

On closer examination of the material types, it became clear that the information was not very detailed and no additional information could be added about the type of material, other than the above categories.

Thiele
Does not sell via the website and does not display individual spectacles /material types on the website.

Louis Nielsen
On Louis Nielsen's website (louisnielsen.dk/briller), there were 950 different spectacles in their range (including 88 sunglass frames) at the time of the search. Of the 950 frames, 72 frames were for children, 6 frames for "teens" and 872 frames for adults (430 frames for women and 442 frames for men).

Louis Nielsen's range of frames for children (including frames for "teens") consisted of 72 + 6 frames of 9 different brands. These were in the price range: DKK 495 - <1095, where the brands Specsavers and Disney were the cheapest and Specsavers also the most expensive (DKK 1295). The most expensive frames for children and young people were all made of titanium.

Louis Nielsen's range for adults consisted of a total of 842 spectacle frames. These were in the price range: DKK 195 - 1895. The cheapest frames were from the brand Specsavers, and the most expensive were from brands such as Adidas, HUGO, Gant and Lyle & Scott.

The description of the spectacles on the website varies considerably. Some spectacles are described with colour and different materials, and other spectacles are described very sparingly. On the website, it was not possible to search for spectacle frames based on material, and therefore it was not possible to make an overview of the different types of material.

Profil Optik
On Profil Optik's website (profiloptik.dk/briller), there were 1478 different frames for adults, 70 frames for children and 53 frames in the category "youth" at the time of the search. The spectacle frames for adults included over 50 different brands and were in the price range DKK 200 – 6450. The most expensive brands (DKK > 6000) were Giorgio Armani and Gucci, and the cheapest were of the brand D. Arnesen.

For children, there were 7 different brands in the price range: DKK 200 – 3500, where the brand Lindberg was the most expensive (DKK >1750), and D. Arnesen the cheapest at DKK 200.

It was not possible to get an overview of the different types of material on the website. However, it was possible to see which frames were most popular in both the adult and children's categories. An overview of spectacle frame material in the top 30 for adults and children, respectively, can be found in TABLE 1 and TABLE 2.

TABLE 1. The 30 best-selling frames for adults (source: ProfilOptik.dk)

Type	Material	Colour	Price (dkk)
Reading spectacles	Metal (2 types)	Blue, gold	250
Reading spectacles	Nylon (7 types)	Brown, variegated, blue and black	250
Reading spectacles	Not specified (4 types)	Brown/variegated, gold and black	300
Common	Acetate (13 types)	Variegated, gold, unspecified, brown, variegated black/brown, transparent, gold, green, black, variegated/brown	590-3500
Common	Metal (3 types)	Gold/rose, silver	790-590
Common	Metal (1 types)	Red	4550

TABLE 2. The 30 best-selling spectacle frames for children (source: ProfilOptik.dk)

Type	Material	Colour	Price (dkk)
Common	Metal (12 types)	Green, brown/variegated, brown, transparent, gold, rose	650-700
Common	Acetate (18 types)	Brown, transparent, grey, green, brown/variegated, blue, red, rose/transparent.	700-1400

Summary

When searching for materials used for spectacle frames on the four different websites, it became clear that information regarding spectacle materials was very sparse and in many cases it was not provided. In some cases, the information was misleading. In general, the descriptions of spectacle frames on the websites of various opticians were not more detailed for spectacle frames in higher price ranges than in lower price ranges. In many cases, on opticians' websites, the material was listed as 'plastic', which is a very broad category. An optometrist chain stated on a website that they often use 'acetate' as a common term for their plastic materials, which must be considered misleading, as acetate is a specific type of plastic and does not cover plastic in general. Frames made of metal materials were most often not elaborated, but simply stated as "metal". The fact that the material is described as "metal" must be regarded as being very uninformative, as the term metal can cover many different elements and alloys. In addition, there are typically also temple tips made of another material than metal, and nose pads on the spectacle frames, the material of which is often not described on the website.

3.2.2 Other spectacle retailers and their range of spectacles

Danish consumers can also buy spectacles in retail and web-based shop. A selection of the web-based dealers has been surveyed for information regarding materials.

General shops

As reading spectacles are sold in both opticians' shops and also in more general shops, a screening of spectacle frame materials was carried out in various retail shops. This screening only included reading spectacles for adults. TABLE 3 shows an overview of the websites examined.

TABLE 3. Information about spectacle materials from the retail trade

Shop website	Information about spectacle materials
Harald-nyborg.dk (Harald Nyborg)	a) Has 2 types of reading spectacles b) Spectacles made of 'plastic' material. Colour black/shiny black c) Spectacles of several materials; 'metal' and 'plastic'.
Matas.dk (Matas)	Sells reading spectacles of the brand Prestige. No material information on the website.
Apoteket.dk (Apoteket)	Sells reading spectacles of the brand Nomeco. No material information on the website.
Flyingtiger.com (FlyingTigerCopenhagen)	Markets 5 different reading spectacles. Three of plastic and 2 of metal with nose pad and temple tips. The frames are in the colours black, gold, beige, grey and/or white. No information about the material.
Sostrenegrene.com (Søstrene Grene)	Several different reading spectacles are stated to be made of 'polycarbonate' material (the only frames in the survey stated to be made of polycarbonate).

All spectacles identified on these websites were of the type reading spectacles and were in the price range below DKK 100. On several of the websites, it was possible to buy 3-pack reading spectacles. Harald Nyborg and Søstrene Grene were the only ones to provide the material for spectacles.

Websites investigated that did not include the sale of spectacles:

- Silvan
- Bauhaus
- XL Byg
- Din Isenkræmmer
- Bilka
- Føtex

Web-based shops

In connection with this project, a screening of web-based shops was also carried out to determine whether they offer other spectacle materials than those already identified. In the screenings, cellulose propionate (SmartBuyGlasses.dk) and carbon fibre (fleyecopenhagen.com) were found, in addition to the already identified material types.

3.2.3 Recycled plastic

Since the survey identified recycled plastic as a material type, a separate search was carried out to investigate which type of plastic recycled plastic typically is, as well as the market share of spectacles made of recycled plastic. Frames made of recycled plastic were found on the following websites:

- Ojeoje.dk. Uses plastic from transparent or coloured plastic packaging from food, bottles and screw caps. Claimed to be 100% free of BPA and phthalates.
- MonkeyGlasses.dk. Manufactures blue light and reading spectacles in "Upcycled Glasses", which are 'made from 100% recycled, certified plastic from food containers and plastic bottles'.
- Profil Optik.dk. Offers eyewear by the brand Fellipini and their collection called Sea2see. Sea2See is claimed to be spectacles made of 100% recycled ocean plastic that is collected by fishermen in the Mediterranean.
- Lensway.dk. Sells five-one frames, which means that 5 PET bottles become 1 frame, and natural dyes are used.

3.2.4 Identified material types

Spectacles on the Danish market in 2023 primarily occur in two different material categories: plastic and metal. In addition to the two categories, the project has identified frames made of wood, bamboo and horn. However, these are few in number.

The industry has been contacted in connection with the survey. Two of the major players have provided information about their sales estimates for different materials (via email and telephone contact). This knowledge, as well as information gathered via web searches, is included in the assessment of the market share of the identified material types for spectacle frames on the Danish market in 2023. The market share is given as low, medium or high.

TABLE 4. Material types for spectacle frames and their market share

Material category	Material type	Market share
Plastic	Acetate[A]	High
	Cellulose Propionate	Medium
	Recycled plastic	Medium
	Carbon fibre/carbon wood	Medium
	Nylon	Medium
	Polycarbonate	Low[B]
	Polyetherimide (PEI) (Ultem)	Low
	Plastic (unknown)	High
Metal (alloy)	Aluminium	Low
	Titanium	Medium
	Magnesium	Low
	Stainless steel	Low
	Gold	Low
	Metal (unknown)	High
Other	Wood	Low
	Bamboo	Low
	Horn	Low

3.3 Identification of problematic substances in spectacle frames

Plastic materials contain polymers and a number of substances, some of which can be considered impurities, and others are deliberately added substances. These can migrate to the environment with which the plastic material is in direct contact.

The substances of concern for this project are chemical substances with critical, systemic effects (e.g. with carcinogenic, mutagenic, reproductive or endocrine disrupting effects) and skin sensitising properties, i.e. a substance is considered problematic if it has one or more of the following CLH classifications[8]: carcinogenicity, mutagenicity, reproductive toxicity and/or skin sensitising (Carc., Mut., Repr., Skin sens).

To identify which problematic substances may be present in spectacle frames, the following activities have been carried out:

- Conducted a search in DHI's plastic material database
- Conducted a literature search
- Contacted the National Allergy Research Centre
- Contact with the industry (see introduction to Chapter 3)

3.3.1 DHI's Plastic Material Database

DHI A/S has developed a validated migration model to estimate the migration of different substances from plastic materials to recipients such as air, food, water, etc. This internal database contains, among other things, a material database for plastic types, which is a library of different plastic materials and their specific content of constituents. The database does not include dyes.

The survey of material types for spectacle frames identified the types of plastic used for spectacle frames. The ingredients for each of the identified types of plastic have been extracted from DHI's database. The extracted information contains an overview of chemical substances that can occur in the different types of plastics and includes both impurities and chemical substances that have been deliberately added.

The list below shows the types of plastic identified in the survey of material types for spectacle frames (section 3.2). The types of plastic that are included in DHI's database and for which the potential ingredients have been identified are marked in bold.

- Acetate
- Cellulose propionate (Determinations from DHI's database do not indicate any problematic substances and therefore there is no table for this material).
- Recycled plastic
- Carbon fibre/carbon wood
- Nylon
- Plastic (unknown)
- Polycarbonate
- Polyetherimide (PEI) (Ultem)

The material 'carbon fibre/carbon wood' is not included in DHI's database, and therefore a search could not be made for chemical substances in this material.

Likewise, 'plastic (unknown)' is not a type of plastic, but a term that covers plastic in general. This is too non-specific for it to be possible to make a search in DHI's database, but since the specific types of plastic on the Danish market have been surveyed, it is assessed that the other types of plastic may very well cover spectacle frames made of unknown plastic. In the project's analyses, several spectacle frames of unknown plastic type have been purchased, which will contribute to knowledge about any other types of plastic in this category.

[8] The CLP Regulation (EU Regulation No. 1272 of 2008) is the applicable EU legislation for the classification and labelling of chemical substances and mixtures. CLP is the abbreviation for "Classification, Labelling and Packaging"

Recycled plastic, like 'plastic (unknown)', is not a type of plastic, but a term that covers recycled plastic in general. However, DHI's database includes data for recycled plastic for cosmetic packaging collected from Danish stakeholders (Environmental Project No. 2174). A search of these has been made, but it is estimated that recycled plastic may very well consist of plastic types that have already been identified in the survey. In the project's analyses, several frames made of recycled plastic, consisting of unknown plastic, have been purchased, which will contribute to knowledge about any other types of plastic in this category.

The ingredient substances have been extracted from the database for each of the types of plastic marked in bold above. As substances of concern are chemical substances with critical, systemic effects (e.g. with carcinogenic, reproductive or endocrine disrupting effects) and skin-sensitising properties, DHI's database was searched for chemical substances with one or more relevant harmonised classifications in the CLP Regulation. As these classifications are particularly relevant compared to other CLH classifications, these are highlighted in **bold** in the tables below.

TABLE 5. Chemical substances of concern found in DHI's database for the plastic material acetate

CAS No.	Substance name	Harmonised classification
84-65-1	Anthraquinone	**Carc. 1B H350**
1344-37-2	Lead sulfochromate yellow	**Car. 1B H350; Repr. 1A H360Df**; STOT RE 2 H373; Aquatic Acute 1 H400; Aquatic Chronic 1 H410
126-73-8	Tributyl phosphate	**Carc. 2 H351**; Acute Tox. 4 H302; Skin Irrit. 2 H315
115-96-8	Tris(2-chloroethyl) phosphate	**Carc. 2 H351; Repr. 1B H360F;** Acute Tox. 4 H302; Aquatic Chronic 2 H411
84-74-2	Dibutyl phthalate	**Repr. 1B H360Df**; Aquatic Acute 1 H400

There is no table for the cellulose propionate material, as no problematic substances have been found in the material, according to the criteria above.

TABLE 6. Chemical substances of concern found in DHI's database for the plastic material recycled plastic

CAS No.	Substance name	Harmonised classification
117-81-7	Bis(2-ethylhexyl) phthalate (DEHP)	**Repr. 1B H360FD**
13048-33-4	1,6-Hexanediol diacrylate (HDDA)	Skin Irrit. 2 H315; Eye Irrit. 2 H319; **Skin Sens. 1 H317**
615-05-4	2,4-Diaminoanisole	**Carc. 1B H350; Muta. 2 H341**; Acute Tox. 4 H302; Aquatic Chronic 2 H411
95-80-7	2,4-Diaminotoluene	**Carc. 1B H350; Muta. 2 H341; Repr. 2 H361f;** Acute Tox. 3 H301; Acute Tox. 4 H312; STOT RE 2 H373; **Skin Sens. 1 H317;** Aquatic Chronic 2 H411
90-04-0	2-Methoxyaniline	**Carc. 1B H350; Muta. 2 H341**; Acute Tox. 3 H331; Acute Tox. 3 H311; Acute Tox. 3 H301
71868-10-5	2-Methyl-4'-(methylthio)-2-morpholinopropiophenone	**Repr. 1B H360FD;** Acute Tox. 4 H302; Aquatic Chronic 2 H411
91-94-1	3,3'-Dichlorobenzidine	**Carc. 1B H350**; Acute Tox. 4 H312; **Skin Sens. 1 H317**; Aquatic Acute 1 H400; Aquatic Chronic 1 H410
101-77-9	4,4'-Diaminodiphenylmethane (MDA)	**Carc. 1B H350; Muta. 2 H341;** STOT SE 1 H370; STOT RE 2 H373; **Skin Sens. 1 H317**; Aquatic Chronic 2 H411
106-47-8	p-Chloroaniline	**Carc. 1B H350;** Acute Tox. 3 H331; Acute Tox. 3 H311; Acute Tox. 3 H301**; Skin Sens. 1 H317**; Aquatic Acute 1 H400; Aquatic Chronic 1 H410

CAS No.	Substance name	Harmonised classification
95-69-2	4-Chloro-o-toluidine	**Carc. 1B H350; Muta. 2 H341**; Acute Tox. 3 H331; Acute Tox. 3 H311; Acute Tox. 3 H301; Aquatic Acute 1 H400; Aquatic Chronic 1 H410
119-61-9	Benzophenone	**Carc. 1B H350**
85-68-7	Benzyl-butylphthalate	**Repr. 1B H360Df**; Aquatic Acute 1 H400; Aquatic Chronic 1 H410
77-90-7	Co-elution, Tributyl acetyl citrate and saturated alkane	Flam. Gas 1 H220; Press. Gas; **Carc. 1A H350; Muta. 1B H340**
84-74-2	Dibutylphthalate	**Repr. 1B H360Df**; Aquatic Acute 1 H400
84-69-5	Diisobutylphthalate	**Repr. 1B H360Df**
78-59-1	Isophorone	**Carc. 2 H351**; Acute Tox. 4 H312; Acute Tox. 4 H302; STOT SE 3 H335; Eye Irrit. 2 H319
138-86-3	Limonene	Flam. Liq. 3 H226; Skin Irrit. 2 H315; **Skin Sens. 1 H317**; Aquatic Acute 1 H400; Aquatic Chronic 1 H410
91-20-3	Naphthalene	**Carc. 2 H351**; Acute Tox. 4 H302; Aquatic Acute 1 H400; Aquatic Chronic 1 H410
95-53-4	o-Toluidine	**Carc. 1B H350**; Acute Tox. 3 H331; Acute Tox. 3 H301; Eye Irrit. 2 H319; Aquatic Acute 1 H400
69-72-7	Salicyclic acid	**Repr. 2 H361d**; Acute Tox. 4 H302; Eye Dam. 1 H318
42978-66-5	Tri(propylene glycol) diacrylate	STOT SE 3 H335; Skin Irrit. 2 H315; Eye Irrit. 2 H319**; Skin Sens. 1 H317**; Aquatic Chronic 2 H411
77-94-1	Tributyl citrate	Flam. Gas 1 H220; Press. Gas; **Carc. 1A H350; Muta. 1B H340**
15625-89-5	Trimethylolpropane triacrylate	**Carc. 2 H351**; Skin Irrit. 2 H315; Eye Irrit. 2 H319; **Skin Sens. 1 H317**; Aquatic Acute 1 H400; Aquatic Chronic 1 H410
101-77-9	4,4'-diaminodiphenylmethane (MDA)	**Carc. 1B H350; Muta. 2 H341**; STOT SE 1 H370; STOT RE 2 H373; **Skin Sens. 1 H317**; Aquatic Chronic 2 H411

TABLE 7. Chemical substances of concern found in DHI's database for the plastic material nylon

CAS No.	Substance name	Harmonised classification
12179-04-3	Sodium tetraborate pentahydrate	**Repr. 1B H360FD**
1303-86-2	Boron oxide	**Repr. 1B H360FD**
1309-64-4	Antimony trioxide	**Carc. 2 H351**
1330-43-4	Sodium borate, decahydrate	**Repr. 1B H360FD**
84-65-1	Anthraquinone	**Carc. 1B H350**

TABLE 8. Chemical substances of concern found in DHI's database for the plastic material polycarbonate

CAS No.	Substance name	Harmonised classification
1344-37-2	Lead sulfochromate yellow	**Carc. 1B H350; Repr. 1A H360Df**; STOT RE 2 H373; Aquatic Acute 1 H400; Aquatic Chronic 1 H410
12656-85-8	Lead chromate molybdate sulfate red	**Carc. 1B H350; Repr. 1A H360Df;** STOT RE 2 H373; Aquatic Acute 1 H400; Aquatic Chronic 1 H410
13463-67-7	Titanium dioxide	**Carc. 2 H351** (Inhalation)

TABLE 9. Chemical substances of concern found in DHI's database for the plastic material polyetherimide (PEI/Ultem)

CAS No.	Substance name	Harmonised classification
80-05-7	Bisphenol A	**Repr. 1B H360F**; STOT SE 3 H335; Eye Dam. 1 H318; **Skin Sens. 1 H317**; Aquatic Acute 1 H400; Aquatic Chronic 1 H410
108-45-2	m-Phenylenediamine	**Muta. 2 H341**; Acute Tox. 3 H331; Acute Tox. 3 H311; Acute Tox. 3 H301; Eye Irrit. 2 H319; **Skin Sens. 1 H317**; Aquatic Acute 1 H400; Aquatic Chronic 1 H410
85-44-9	Phthalic anhydride	Acute Tox. 4 H302; STOT SE 3 H335; Skin Irrit. 2 H315; Eye Dam. 1 H318; Resp. Sens. 1 H334; **Skin Sens. 1 H317**

Two of the substances in the above tables are not considered to be relevant to the present project, as their use is prohibited in spectacle frames, according to the Executive Order on Lead. These are the following substances:

- Lead chromate molybdate sulfate red, CAS nr. 12656-85-8
- Lead sulfochromate yellow, CAS nr. 1344-37-2.

3.3.2 Literature search

A literature search has been conducted to identify which problematic substances have previously been found in spectacle frames or have been linked to contact allergy after the use of spectacles. This was done to identify studies, reports and previous analyses, etc., with information about spectacle materials and findings of problematic chemical substances.

The focus of the literature search has been to identify non-regulated chemical substances of concern. As the problem of nickel in spectacle frames is known and regulated, studies that only deal with allergy cases caused by nickel were not included in the literature search.

The search did not identify previous reports that shed light on the topic of problematic chemical substances in spectacle frames. In order to identify previous analyses of problematic substances and previous cases of confirmed contact allergy after wearing spectacles, a search was made for relevant scientific articles in PubMed.

Search in PubMed

In order to identify relevant information about problematic substances in spectacle frames, a search has been carried out in PubMed. Many problematic substances that are expected to be present in different types of plastic for spectacle frames have already been identified via DHI's database (section 3.3.1). However, the database does not include dyes and the literature search may be able to supplement the identified substances from the database.

The search was conducted in Pubmed with the following keywords for the title and/or abstract:

eyeglass; spectacle frame; spectacles; contact dermatitis; sensi*; allerg*; eczema; elicitation; ACD; CD; problematic; carc*; toxi*; repr*; endocrine disrup*.*

Thus, data were searched for problematic substances with critical effects (carcinogenic, reproductive and/or endocrine disrupting effects) as well as skin sensitising properties linked to spectacles.

The search in PubMed resulted in findings regarding skin sensitising substances linked to spectacles. No studies for the critical effects were identified.

The identified publications were sorted using the following review:

- Title review
- Review of abstract
- Review of the publication.

In the review of the literature, the reference lists in relevant publications were reviewed for other relevant references.

Three articles of particular relevance were identified on contact allergy after the use of spectacle frames in Denmark:
- Ahrensbøll-Friis et al. 2021
- El Houri et al. 2016
- Andersen et al. 2013.

In addition, a previous review of contact allergy with the use of spectacles (Nakada & Maibach 1998) was found, as well as several case studies from other countries, primarily Japan.

The relevant references are reviewed below. Ahrensbøll-Friis et al. (2021) and Nakada & Maibach (1998) are described in separate sections. El Houri et. (2016) and Andersen et al. (2013) are included in the Case Studies section.

The skin-sensitising chemical substances are divided as far as possible into chemical groups that describe their function:
- metals
- plastic components
- plasticizers
- solvents
- UV stabilizers
- antioxidants
- dyes
- waxes.

Ahrensbøll-Friis et al. (2021)
In 2021, the National Allergy Research Centre published a scientific article on patients referred to their department due to suspected contact allergy when wearing spectacles in the period 1 January 2017 to 31 March 2021. Of these, 19 patients were tested with a patch sample containing the European basic series, a series for spectacles developed at the Department of Skin and Allergy at Gentofte University Hospital (individual substances not stated), 26 perfume substances and selected allergenic dyes (not stated), based on the National Allergy Research Centre's previous experience with chemical analyses of a spectacle temple.

Six of the 19 patients had developed contact allergy behind the ear, five at the temple and four on the bridge of the nose. Of the 19 patients, seven patients had positive patch samples for a dye. The results from the study are presented in TABLE 10.

The seven patients who tested positive for contact allergy to dyes wore either black or tortoise-shell-coloured spectacle frames. Five patients had used a plastic frame, and two patients had used metal spectacles made of titanium with plastic on the temple tip.

TABLE 10. Data from Ahrensbøll-Friis et al. (2021)

Sub-stance group	Chemical substance	Location	Eyewear material (colour)	Patient nr.
Metals	Nickel sulfate	Behind the ear, on the cheeks and bridge of the nose	Plastic (tortoiseshell)	2[B]
		Bridge of the nose	N/A (tortoiseshell)	5[B]
Dyes	C.I. Solvent Yellow 1	In areas in contact with spectacles	Plastic - 3 different kinds (black)	4[A,B,C]
	Disperse Orange 3	In areas in contact with spectacles	Plastic - 3 different kinds (black)	4[A,B,C]
	Solvent 60 (CAS no. 6925-69-5; SO60)	In skin areas in contact with spectacle frames	Plastic (tortoiseshell)	1[A]
		Behind the ear, on the cheeks and bridge of the nose[B]	Plastic (tortoiseshell)	2[B]
		In areas in contact with spectacles	Plastic - 3 different kinds (black)	4[A,B,C]
		Bridge of the nose	N/A (tortoiseshell)	5[B]
		Around the eyes, behind the ears, on the bridge of the nose, as well as the forehead and cheeks	Plastic – 2 pcs. (tortoiseshell)	7
	Solvent Yellow 14	Behind the ear	Titanium frame with black coloured plastic cover on temple tip	3[B]
		In areas in contact with spectacles	Plastic - 3 different kinds (black)	4[A,B,C]
		Face and behind the ears	Black-coloured titanium with black plastic temple tips	6[B] – from the temple tip
		Around the eyes, behind the ears, on the bridge of the nose, as well as the forehead and cheeks	Plastic – 2 pcs. (tortoiseshell)	7

[A]: The patient had previously experienced dermatitis.

[B]: Was tested for scrapes from spectacle frames, with a positive patch test.

[C]: The patient previously showed a positive patch test with para-phenylamine, and the positive patch tests with dyes may be associated with this.

The content of Solvent Yellow 14 was confirmed by chemical analysis of a spectacle frame (patient 3).

The study did not investigate whether patients were allergic to CI Solvent Red 179 (SR179), but the authors suggested including this dye in patch tests for patients with contact allergy after wearing spectacles.

Nakada & Maibach (1998)

Nakada & Maibach (1998) is a review of published allergy cases after wearing spectacles. The study thus forms an overview of published allergy cases in the period up to the year 1994.

The positive test results for contact allergy are reported for the years 1937-1994 and must therefore be considered to be of older date and are not necessarily representative of spectacle frames on the current Danish market. However, the relevance of the chemical substances cannot be excluded, but they are confirmed if they occur in other relevant studies.

The study includes allergy cases recorded in two periods: period A up to 1985; period B 1986-1996. The study for period A (-1985) includes:

- Number of patients
- Year
- Chemical substance.

For period B (1986-1994), additional data are included:

- Number of patients
- Year
- Age and gender of the patient
- How long the patient has had a skin allergy to the specific area of skin
- Results from the positive patch test
- Chemical substance.

Data from the study are reproduced in TABLE 11, in which all positive patch tests are also shown. For positive patch samples from the year 1986 onwards, the geography (country) is noted, as well as the area of skin where the allergy occurs, e.g. 'behind the ear' and 'bridge of the nose'. For years where several patients tested positive for the same allergen, the number of positive patients is indicated in brackets next to the year. Cases where the allergen is not stated are not included in the table.

TABLE 11. Data from Nakada & Maibach (1998). Chemical substances identified as allergens. No information about eyewear material in reference.

Substance group	Chemical	Land	Year	Number of patients	Location of eczema
Metals	*Cobalt*	-	1980	1	-
	Nickel	-	1961	1	-
		-	1966 (2)	2	-
		-	1976	1	-
		-	1978	1	-
		-	1979	1	-
		-	1980 (4)	4	-
		-	1982	1	-
		Taiwan	1987	1	Face
		China	1991	1	Face
Plastic components	*Butyl acrylate*	-	1978	1	-
	Cellulose acetate	-	1980	1	-
	Epoxy resin	-	1976	1	-
	Phenol-formaldehyde, rubber	-	1959	1	-
Plasticizers	*Abietic acid*	SE	1994	1	Behind the ear, nose and cheeks
	Diethyl phthalate	UK	1991	1	Temple and behind the ear
	Tricresyl phosphate	-	1938	1	-
	Triphenyl phosphate	-	1938	1	-
		-	1966	1	-

Substance group	Chemical	Land	Year	Number of patients	Location of eczema
		DK	1986	1	Bridge of the nose and temple
	Tritolyl phosphate	-	1966	1	-
Solvents	*Ethylene glycol monomethyl ether acetate*	-	1971	1	-
	Methylethylketone	-	1966	1	-
UV stabilizers	*Resorcinol monobenzoate*	-	1972 (3)	3	-
		-	1975	1	-
		-	1983	1	-
	Phenyl salicylate	-	1983	1	-
		UK	1986	1	Behind the ear, at the top of the cheeks
		UK	1986	1	Behind the ear
Antioxidants	*p-tert-butyl-phenol?*	-	1972	1	-
Dyes	*Anthraquinone*	-	1981	1	-
	Solvent Red 481	-	1980	1	-
	Solvent Red 26	-	1972	1	-
	Solvent Yellow 3	-	1972	1	-
	p-aminophenol	-	1939	1	-
		-	1961	1	-
	p-phenylenediamine	-	1939, 1966	1	-
		Australia	1988	1	Side of bridge of nose, at eyebrows, lower eyelids, behind ear.
	Brown-black dye	-	1943	1	-
Waxes	*Aliphatic isocyanate*	-	1987	1	Side of the nose
	Turpentine	-	1972	1	-

Of the allergens identified, plasticizers and UV stabilizers were rated as the most common allergens in recent years (except in China and Taiwan, where nickel is a dominant allergen).

Case studies, including El-Houri et al. (2016) and Andersen et al. (2013)
In the literature, there are several case studies describing contact allergy and patch tests for a single patient. The literature search resulted in four such case studies. These are presented in TABLE 12. For the four cases, a patch test has been made with scrapes from the spectacle frames, which has been positive.

TABLE 12. Case studies of contact allergy to one chemical substance when wearing spectacles

Substance group	Chemical substance	Land	Year	Location	Eyewear material (colour)	Reference
Dye	Solvent Orange 60 (Identified in eyewear material)	Japan	2016	Behind the ears	Plastic (reddish/brownish)	Shono et al. 2017
		Japan	2017	Behind the ears	Metal spectacles with plastic on the temple tips	Shono & Kania 1999
	C.I. Solvent Red 179	Japan	2001	Over the ears	Unknown goggle material with plastic on the temple tips (red/violet)	Tsunoda et al. 2001
Preservative	Methylisothiazolinone (MI) CAS No. 2682-20-4	DK	2016	-	Unknown	El-Houri et al. 2016
Plasticizer	Triethylene glycol bis(2-ethylhexanoate) CAS No. 94-28-0	DK	2013	Forehead, and other places on the body.	Plastic (black)	Andersen et al. 2013

In addition to the above case studies, two case studies were identified, each of which included a patient who tested positive for several chemical substances.

Batchelor & Wilkinson (2006)

One case study describes a man who had positive patch tests for a wide range of chemical substances. The contact allergy appeared around his ears after the temple tips on his spectacle frames had been replaced by new plastic ends. He was tested for several different series, including plastic, formaldehyde, epoxy and textile, and tested positive for a wide range of chemical substances. The results of the positive patch tests are shown in TABLE 13.

TABLE 13. Chemical substances, patient from the Batchelor & Wilkinson (2006) case study, tested positive for contact allergy

Substance group	Substance name
Waxes	Colophonium
	Turpentine oil
Plasticizers	Abietic acid
Dyes	p-Phenylenediamine
	Aminoazobenzene
	Disperse Orange 3
	Disperse Yellow 3
	Disperse Red 1
	Disperse Red 17
	Disperse Blue 3
	Disperse Blue 35
	Disperse Blue 124
	Disperse Blue 153
	Disperse Brown 1
	Disperse Blue 106
	Direct Orange 34
	4-Aminophenol

The above table shows positive patch samples for 17 different chemical substances, and the authors also mentioned the possibility that there were positive cross-reactions to unidentified dyes. The case study did not describe a patch sample of scrapes from the spectacles or identification of the chemical substances in the spectacles.

Crépy et al. (2011)
The second case study of a patient who was allergic to several chemical substances concerns a woman who had developed depigmentation after wearing spectacles. The depigmentation occurred where the temples had had skin contact. Patch samples with the European basic series, a plastic and adhesive series and basic materials from spectacle frames showed positive reactions to PTBC, p-tert-butylphenol, PTBF, tert-butyl hydroquinone and a mixture of methylchloroisothiazolinone and methylisothiazolinone. Two months after the patch test, there was depigmentation in the areas where the woman had been tested for PTBC, PTBP, PTBF and tert-butyl hydroquinone. The depigmentation disappeared again slowly (5 months). Chemical content analyses of the lacquer on the spectacles showed it contained PTBP, dimethyl phthalate and diethyl phthalate and not the other chemical substances for which the patient tested positive.

The authors estimate that the depigmentation was probably caused by PTBP, but depigmentation had also been seen for skin contact with other chemical substances. Since the lacquer and the spectacles themselves had been tested, relevant chemical substances could be narrowed down to be the chemical substances that appear in TABLE 14:

TABLE 14. Chemical substances for which patients from the case study Crépy et al. (2011) tested positive (detected in spectacles used)

Substance group	Fabric name
Antioxidant	p-tert-Butylcatechol (PTBC)
Plasticizers	Dimethyl phthalate
	Diethyl phthalate

Problematic substances in metal
As nickel is already covered by the chemical regulation, literature on nickel is not included in this report, as it focuses on unregulated chemical substances of concern.

In the literature search, studies were found on problematic substances in skin contact with metal components on the spectacle frames. One study investigated the migration of beryllium and copper from a temple and whether this could result in skin absorption (Magnano et al. 2022). In addition, a study with palladium (Connolly et al. 2001) and chromium (Kim 2013) was identified. An overview of identified problematic substances in metal eyewear materials can be found in TABLE 15.

TABLE 15. Problematic substances previously studied in metal eyewear material (excl. nickel)

Substance group	Substance name	CLH Classification
Metals	Beryllium	Skin Sens. 1; H317 Carc. 1B
	Copper	None relevant
	Palladium	None
	Chromium	None

Other allergy cases when wearing spectacles
The literature search also revealed allergic cases from chemical substances on and in the lenses themselves. This concerned the chemical substances radon (Fleisher et al. 2001; Haley et al. 2000) and PFAS (Herkert et al. 2022). In addition, there were also cases of allergy from protective spectacles (Telary et al. 1994; Navarro-Trivi et al. 2021).

3.3.3 Contact with the National Allergy Research Centre

The National Allergy Research Centre was contacted as part of the identification of material types and problematic substances.

The National Allergy Research Centre is a national centre established by the Danish Environmental Protection Agency in 2001 to learn more about the health effects of chemical substances. The National Allergy Research Centre has been established in a collaboration between the Department of Skin and Allergy at Gentofte University Hospital and the Department of Skin and Allergy at Odense University Hospital.

The purpose of the National Allergy Research Centre is to prevent allergy to chemical substances in consumer products through research, monitoring and advice. The tasks include determining the causes of contact allergy, which products, substances and concentrations cause allergy, as well as which levels do not cause disease, so that these can be implemented in legislation.

As the National Allergy Research Centre sees patients with facial eczema and has previously published a scientific article on the subject, the department at Gentofte University Hospital was contacted.

The National Allergy Research Centre has continuously contributed knowledge to the survey and has, among other things, provided information about which chemical substances they test with when patients with contact allergy from the use of spectacle frames need to be patch tested. All patients are routinely tested with about 30 allergenic substances, which are part of the so-called European basic series, which European dermatologists recommend that they be tested with as a minimum if contact allergy is suspected[9]. In addition to this, the National Allergy Research Centre has prepared a list of substances that are considered relevant for testing for allergenic ingredients in spectacle frames, which is stated in TABLE 16.

TABLE 16. Testing for allergenic substances in spectacle frames (National Allergy Research Centre)

Substance name	CAS No.
Solvent Orange 60	6925-69-5
Solvent Yellow 14/Sudan I	842-07-9
Solvent Red 179	6829-22-7
Diethylhexyl phthalate	117-81-7
Turpentine oil oxidized[A]	68917-66-8
Bis(2,2,6,6-tetramethyl-4-piperidyl) sebacate	52829-07-9
4,4-Diaminodiphenylmethane (MDA)	101-77-9
Butyl acrylate	141-32-2
Resorcinol monobenzoate	136-36-7

[9] Diagnosis – National Allergy Research Centre

Substance name	CAS No.
p-tert-butylphenol	98-54-4
Tricresyl Phosphate	1330-78-5

[A]: Oxidized vegetable turpentine is stated to contain the hydroperoxides of turpentine oil, with the primary allergens being the hydroperoxides of delta-3-carene and alpha-pinene.

3.3.4 Summary, identification of problematic substances in spectacle frames

In the survey of problematic substances in spectacles, a large number of problematic substances have been identified that can potentially occur in plastic spectacle materials.

The search in DHI's database, contact with the National Allergy Research Centre and the literature search have identified a number of chemical substances that could be relevant to investigate further in terms of their content and migration in plastic spectacle frames. These chemical substances are shown below, broken down into two different tables: TABLE 17 includes dyes, and TABLE 18. the other chemical substances. This division has been made because the chemical analyses do not allow screening for dyes by GC-MS in the same way as most other chemical substances. The analyses for dyes require, among other things, a different method of analysis with reference substances.

Some of the dyes that have previously been shown to cause contact allergies do not have a CLH classification as a skin sensitiser. Therefore, it was checked whether the identified dyes in the survey are included in Annex XV, the restriction report on skin sensitising substances in textiles, leather and fur (ECHA 2019). This restriction proposal contains a large number of chemical substances with skin sensitising properties that are not CLH classified.

In this project, a number of specific dyes have been selected that are included in the chemical analyses (described further in phase 2). The selection of dyes included in the chemical analyses has been made in consultation with the Danish Environmental Protection Agency. The identified dyes, as well as those selected for the analyses, are shown in TABLE 17.

Two of the problematic substances identified using DHI's database are not included below, as their use is prohibited in spectacle frames according to the Executive Order on Lead: lead chromate molybdate sulfate red (CAS no. 12656-85-8) and lead sulfochromate yellow (CAS no. 1344-37-2).

Each of the tables contains the following information:

- Substance identifiers; substance name and CAS no.
- Harmonised CLH classifications (relevant CLH classifications are highlighted in bold)
- Candidate List Substance/SVHC Substance (REACH) and Intrinsic Properties
- Substances subject to authorisation that are included in the authorisation list (REACH Annex XIV)[10]
- Restriction list under REACH (Annex XVII). These chemical substances have a limited use, as a single substance, in mixtures or in an article.

[10] SVHCs whose intrinsic properties, volume use or/and distributions require authorisation before use

TABLE 17. Investigation of relevant problematic dyes in plastic spectacles

Dyes selected for chemical analysis are indicated by an X.

CAS No.	Substance name	Harmonised classification	Included in the candidate, authorisation or restriction list	Included in the restriction proposal for selected colouring agents (ECHA 2019)[A]	Source	Included in analytics
106-50-3	p-Phenylenediamine	Skin Sens. 1: H317	-	-	Batchelor & Wilkinson (2006)	X
12222-75-2	CI Disperse Blue 35	-	-	X	Batchelor & Wilkinson (2006)	-
12223-01-7	CI Disperse Blue 106	-	-	X	Batchelor & Wilkinson (2006)	-
1325-54-8/ 12222-37-6	Direct Orange	-	-	-	Batchelor & Wilkinson (2006)	-
23355-64-8	CI Disperse Brown 1	-	-	X	Batchelor & Wilkinson (2006)	-
2475-46-9	CI Disperse Blue 3	-	-	X	Batchelor & Wilkinson (2006)	-
2832-40-8	CI Disperse Yellow 3	Skin Sens. 1: H317 Carc. 2: H351	-	X	Batchelor & Wilkinson (2006)	X
2872-52-8	CI Disperse Red 1	-	-	X	Batchelor & Wilkinson (2006)	-
3179-89-3	CI Disperse Red 17	-	-	X	Batchelor & Wilkinson (2006)	X
60-09-3	Solvent yellow 1 / Amino-azobenzene		Restricted List: Restricted Entry 43 REACH Annex XVII	X	Ahrensbøll-Friis et al. (2021) Batchelor & Wilkinson (2006)	X
61815-13-2	CI Disperse Blue 153	-	-	-	Batchelor & Wilkinson (2006)	-
61951-51-7	CI Disperse Blue 124	-	-	X	Batchelor & Wilkinson (2006)	-
6829-22-7	Solvent Red 179	None Properties of concern: 'A majority of data submitters agree this substance is skin sensitising.'	-	-	National Allergy Research Centre Tsunoda et al. (2001).	X
6925-69-5	Solvent Orange 60	No harmonised clasification. Properties of concern: 'A majority of data submitters	-	-	National Allergy Research Centre Ahrensbøll-Friss et al. (2021) Shono & Kaniwa 1999	X

		agree this substance is skin sensitising.				
730-40-5	Disperse Orange 3		-	X	Ahrensbøll-Friis et al. 2021 Batchelor & Wilkinson (2006)	X
842-07-9	Solvent Yellow 14/Sudan I	Skin sens. 1: H317	-	-	National Allergy Research Centre Ahrensbøll-Friis et al. (2021)	X
84-65-1	Anthraquinone	Carc. 1B H350	-	-	Nakada & Maibach (1998) DHI's database	-

[A] Some dyes that have been shown to cause contact allergies in the past do not have a CLH classification as a skin sensitiser. Therefore, it was checked whether identified dyes in the survey are included in Annex XV, the restriction report on skin sensitising substances in textiles, leather and fur (ECHA 2019). This restriction proposal contains a large number of chemical substances with skin sensitising properties that are not CLH classified.

TABLE 18. Other relevant problematic chemical substances in plastic spectacles

Substances of particular relevance that could be present in the GC-MS screening

CAS No.	Substance name	Harmonised classification	Included in the candidate, authorisation or restriction list	Source
101-77-9	4,4'-Diaminodiphenylmethane (MDA)	Carc. 1B H350; Muta. 2 H341; STOT SE 1 H370; STOT RE 2 H373; Skin Sens. 1 H317	Candidate and approval list: Carcinogenic (Article 57a)	DHI's database National Allergy Research Centre
106-47-8	p-Chloroaniline	Carc. 1B H350; Skin Sens. 1 H317	-	DHI's database
108-45-2	m-Phenylenediamine	Muta. 2 H341; Skin Sens. 1 H317	-	DHI's database
115-96-8	Tris(2-chloroethyl) phosphate	Carc. 2 H351; Repr. 1B H360F	Candidate and approval list: Toxic for reproduction (Article 57c) Included in the restricted list	DHI's database
117-81-7	Bis(2-ethylhexyl) phthalate (DEHP)	Repr. 1B H360FD	Candidate and approval list: Toxic for reproduction (Article 57c) #Endocrine disrupting properties (Article 57(f) - environment) #Endocrine disrupting properties (Article 57(f) - human health)	DHI's database National Allergy Research Centre Nakada & Maibach (1998)[B]
119-61-9	Benzophenone	Carc. 1B H350	-	DHI's database
12179-04-3	Sodium tetraborate pentahydrate	Repr. 1B H360FD	-	DHI's database
126-73-8	Tributyl phosphate	Carc. 2 H351	-	DHI's database
1303-86-2	Boron oxide	Repr. 1B H360FD	Candidate list: Toxic for reproduction (Article 57c)	DHI's database
13048-33-4	1,6-Hexanediol diacrylate (HDDA)	Skin Sens. 1 H317	-	DHI's database

CAS No.	Substance name	Harmonised classification	Included in the candidate, authorisation or restriction list	Source
1309-64-4	Antimony trioxide	Carc. 2 H351	-	DHI's database
131-11-3	Dimethyl phthalate	-	-	Crépy et al. 2011
1330-43-4	Sodium borate, decahydrate	Repr. 1B H360FD	-	DHI's database
1330-78-5	Tricresyl phosphate		-	National Allergy Research Centre
13463-67-7	Titanium dioxide	Carc. 2 H351 (Inhalation)	-	DHI's database
136-36-7	Resorcinol monobenzoate		-	National Allergy Research Centre Nakada & Maibach (1998)[B]
138-86-3	Limonene	Skin Sens. 1 H317	-	DHI's database
141-32-2	Butyl acrylate	Skin Sens. 1 H317 STOT SE 3 H335	-	National Allergy Research Centre Nakada &Maibach (1998)[B]
15625-89-5	Trimethylolpropane triacrylate	Carc. 2 H351; Skin Sens. 1 H317	-	DHI's database
2682-20-4	Methylisothiazolinone (MI)		-	El-Houri et al. (2016)
42978-66-5	Tri(propylene glycol) diacrylate	Skin Sens. 1 H317	-	DHI's database
52829-07-9	Bis(2,2,6,6-tetramethyl-4-piperidyl)sebacate		-	National Allergy Research Centre
60-09-3	C.I. Solvent Yellow I		-	Ahrensbøll-Friis et al. (2021)
615-05-4	2,4-Diaminoanisole	Carc. 1B H350; Muta. 2 H341	-	DHI's database
69-72-7	Salicylic acid	Repr. 2 H361d	-	DHI's database
68917-66-8	Turpentine oil oxidized[A]		-	National Allergy Research Centre Nakada & Maibach (1998)[B]
71868-10-5	2-Methyl-4'-(methylthio)-2-morpholinopropiophenone	Repr. 1B H360FD	Candidate list: Toxic for reproduction (Article 57c)	DHI's database
77-90-7	Co-elution, Tributyl acetyl citrate and saturated alkane	Carc. 1A H350; Muta. 1B H340	-	DHI's database
77-94-1	Tributyl citrate	Carc. 1A H350; Muta. 1B H340	-	DHI's database
78-59-1	Isophorone	Carc. 2 H351	-	DHI's database

CAS No.	Substance name	Harmonised classification	Included in the candidate, authorisation or restriction list	Source
80-05-7	Bisphenol A	Repr. 1B H360F; Skin Sens. 1 H317	Candidate list: Toxic for reproduction (Article 57c) #Endocrine disrupting properties (Article 57(f) - environment) #Endocrine disrupting properties (Article 57(f) - human health) Included in the restricted list.	DHI's database
84-66-2	Diethyl phthalate	-	-	Crépy et al. 2011
84-69-5	Diisobutylphthalate	Repr. 1B H360Df	Candidate and authorisation list: Toxic for reproduction (Article 57c) #Endocrine disrupting properties (Article 57(f) - human health) Included in the restricted list	DHI's database
84-74-2	Dibutyl phthalate	Repr. 1B H360Df	Candidate and authorisation list: Toxic for reproduction (Article 57c) #Endocrine disrupting properties (Article 57(f) - human health) Included in the restricted list.	DHI's database
85-44-9	Phthalic anhydride	Skin Sens. 1 H317	-	DHI's database
90-04-0	2-Methoxyaniline	Carc. 1B H350; Muta. 2 H341	Carcinogenic (Article 57a)	DHI's database
91-20-3	Naphthalene	Carc. 2 H351	-	DHI's database
91-94-1	3,3'-dichlorobenzidine	Carc. 1B H350; Skin Sens. 1 H317	Restricted list	DHI's database
94-28-0	Triethylene glycol bis(2-ethylhexanoate)		-	Andersen et al. 2013
95-53-4	o-Toluidine	Carc. 1B H350	Included in the Candidate List: Carcinogenic (Article 57a)	DHI's database
95-69-2	4-Chloro-o-toluidine	Carc. 1B H350; Muta. 2 H341	-	DHI's database
95-80-7	2,4-Diaminotoluene	Carc. 1B H350; Muta. 2 H341; Repr. 2 H361f STOT RE 2 H373; Skin Sens. 1 H317	Included in the Candidate List: Carcinogenic (Article 57a)	DHI's database
98-29-3	PTBC (p-tert-Butylcatechol)	-	-	Crépy et al. 2011
98-54-4	p-tert-butylphenol	Repr. 2 H361f	-	National Allergy Research Centre Nakada & Maibach (1998)

[A]: Oxidized turpentine is stated to contain the hydroperoxides of turpentine oil. The primary haptens are the hydroperoxides of delta-3-carene and alpha-pinene.

[B]: Listed as turpentine in reference.

3.4 Selection and purchase of spectacle frames for analysis

When selecting spectacles for analysis, it was prioritized to include spectacle frames used by children and adults in colours where allergy cases have been found previously, i.e. black, tortoiseshell, as well as brownish and reddish shades. The survey of material types has helped to make a distribution that represents the market share of the specific materials. In addition, the survey has included prices, and the purchases of the spectacle frames represent, as far as possible, different price ranges.

In connection with the dialogue with the industry, it became possible to get three different acetate samples in optional colours as well as rubber used for temple tips in two different colours. These five different samples are included in the analyses, nos. 16-20.

In agreement with the Danish Environmental Protection Agency, the 20 spectacle frames were purchased, as stated in TABLE 19. However, products no. 16-20 in the table are represented by materials from the manufacturer that are not directly spectacle frames, but the corresponding materials as used in spectacle frames.

TABLE 19. Spectacle frames selected and procured for chemical analysis

Product No.	Colour	Price [A] (DKK/pcs.)	Material according to website	Type of spectacles
1 [B]	Tortoise-shell	505	Plastic	Children's spectacles
2	Tortoise-shell	1150	Unknown	Children's spectacles
3	Black	1800	Recycled plastic	Children's spectacles
4	Tortoise-shell	426	Acetate	Children's spectacles
5	Sort	13,3 (3-pak)	Unknown	Adult spectacles, reading spectacles
6	Tortoise-shell	32,8	Polycarbonate	Adult spectacles, reading spectacles
7	Tortoise-shell	120	Plastic	Adult spectacles, reading spectacles
8	Tortoise-shell	250	Recycled plastic	Adult spectacles, reading spectacles
9	Sort	195	Celluolose propionate	Adult spectacles, reading spectacles
10	Tortoise-shell	877	Propionate	Adult spectacles
11	Sort	2123	Unknown	Adult spectacles
12	Tortoise-shell	3650	Unknown	Adult spectacles
13	Tortoise-shell	2300	Bio-based material	Adult spectacles
14	Tortoise-shell	495	Nylon	Adult spectacles
15	Red	495	Nylon	Adult spectacles
16	Tortoise-shell	-	Acetate Plates	Material for adult spectacles from the manufacturer

Product No.	Colour	Price [A] (DKK/pcs.)	Material according to website	Type of spectacles
17	Brown	-	Acetate Plates	Material for adult spectacles from the manufacturer
18	Red	-	Acetate Plates	Material for adult spectacles from the manufacturer
19	Black	-	Rubber (temple tips)	Material for adult spectacles from the manufacturer
20	Brown	-	Rubber (temple tips)	Material for adult spectacles from the manufacturer

[A] The price stated on the retailer's website when the purchases were made.

[B] Please note, as the delivery time was too long, spectacles no. 1 did not arrive in time to be included in the analyses. Therefore, only product nos. 2-20 were included in the chemical analyses.

3.5 Exposure scenarios

This section lists the exposure scenarios that are considered relevant for the spectacle wearers' potential exposure to chemical substances migrating from the spectacle frames.

Substance exposure per unit surface area

For the further toxicological assessment, it is important to know the extent of the local exposure on the skin surface, i.e. the number of *mg of substance/cm^2 of exposed skin*, as the amount of substance per cm^2 skin is crucial for assessing any risk of developing local skin irritation or skin allergy. For migration tests, it is important to determine the total area of the spectacle frames exposed to migration fluid in order to gain knowledge about the amount of substance that migrated per cm^2 of spectacle frame.

Total quantity of substance released

Furthermore, it is important for the toxicological assessment to determine the extent of the total exposure per day expressed in *mg substance/kg body weight/day*, as this exposure parameter should be used to assess the risk of systemic effects, i.e. effects on the body's function and organs due to the absorption of the substances through the skin and distribution in the body.

Based on the design of the spectacle frames, it is important for the individual spectacle frames in the migration test to estimate how many cm^2 of the frame come into direct contact with the skin, i.e. the area of the inside of the temples, as well as the area of other parts of the frame that come into *contact with the temple + possibly the bridge of the nose, cheeks and forehead.*

For a spectacles wearer, total exposure left on the skin per day can be determined from the results of the migration test:

$$D = M \times A/L$$

where

D: total exposure left on the skin *(mg/kg bw/day)*
M: migrated *amount of substance per cm^2/day* spectacles *(mg/cm^2/day)*
A: Estimated total area of spectacle frames (*cm^2*) in contact with the skin when wearing the spectacles
L: body weight *(kg bw)*

Based on the guidelines associated with the REACH regulation, "Guidance on Information Requirements and Chemical Safety Assessment Chapter R.15: Consumer exposure assessment" (ECHA 2016a), body weights of 60 kg and 70 kg will be used for adult women and men,

respectively. For children's spectacles, it will be assessed which age group the spectacles are intended for, and the body weight for this group will be determined based on growth curves for Danish boys and girls stated by the website *Sundhed.dk* (2023).

In migration testing, it is important to determine the testing conditions (choice of migration fluid, migration time and temperature) so that the amount of substance released represents one day's exposure from the spectacles.

As there is no specific guidance on migration testing in ECHA (2016a), it is considered relevant to use the ISO (2020) guidelines for testing of medical devices, which provide more detailed guidance on migration testing. The following migration design is proposed to best simulate a use case:

Migration fluid: 1:1 ethanol water - as this migration fluid will be able to extract apolar compounds to a greater extent than artificial sweat, corresponding to the fact that there may also be more apolar conditions on the skin, e.g. when using face lotion.

Migration duration: 24 hours (or 72 hours, if necessary, to secure measurable concentrations) - equivalent to maximum use of the spectacles

Temperature: 37 °C - equivalent to the maximum skin temperature

4. Screening analyses

As previously mentioned, the background for this project is that an increasing tendency for facial eczema has been observed for skin contact with spectacles, and that allergic reactions have been observed due to dyes in plastic frames. The starting point for the project has therefore been a focus on allergenic substances in spectacle frames – especially dyes, but at the same time, an investigation of whether there are other relevant substances used in spectacle frames that should be investigated further.

4.1 Analytical issues

The problem with the analysis of dyes is that it is not possible to perform a GC-MS screening analysis to identify the dyes used in spectacle frames. This is because the dyes are not all sufficiently volatile and therefore cannot be analyzed by GC-MS screening. Instead, an LC-MS instrument (in this case LC-MS^2) is used, where liquid chromatography is used for the separation of the substances (Liquid Chromatography). In an LC-MS analysis, the analytical conditions, including settings on the instrument and the selected eluent (the mixture of solvents used for the liquid chromatography), have an impact on how the substances are ionised. Therefore, there is no universal "library" in the same way as in GC-MS, where the dyes can be easily identified via LC-MS^2 from the mass spectra. NIST (National Institute of Standards and Technology), which is behind the commonly used GC-MS library, is continuously working to develop similar libraries for LC-MS, but with a focus on peptides. Small molecules are not supported to the same extent, and NIST's small molecule library for LC-MS^2 instruments with low resolution (not ion-trap) includes only 3,346 compounds[11]. Instead, individual laboratories typically build their own libraries, or purchase libraries with specific groups of substances from the instrument suppliers. Such a library is not available for this project, and it was therefore only possible to identify the dyes by purchasing reference substances and using these for identification and development of the method.

In the project, the chosen approach was therefore to identify the dyes that were potentially used using the survey, after which several of these dyes were selected and purchased as reference substances. An attempt was made to identify the dyes used in the purchased spectacle frames using TLC (thin layer chromatography) as a screening method. TLC distinguishes substances based on their solubility in a liquid and affinity for the surface of the TLC plate. A drop of the dye(s) that had been extracted from each frame was applied to the surface of a TLC plate that binds molecules with different strengths according to their chemical properties, e.g. polarity. When the plate was then placed with the lower part in a liquid (called the mobile phase solvent), the liquid was drawn up through the plate. The distance that each dye migrated up the plate and its appearance on the plate are specific for each dye and can be compared to the purchased reference dyes. The identification of the dyes was thus done visually (with the eyes) and was therefore carried out by an experienced analytical chemist.

The challenge with TLC is that it only gives a tentative identification: for example, it may not be possible to distinguish between two dyes that happen to have the same or similar colour and also the same or similar migration behaviour in the TLC conditions. It should be possible to identify many dyes, but this depends on the individual dyes that are present. As the migration of the dyes up the plate depends on the solvent, among other things, identification of the dyes

[11] https://belong.nist.gov/dokuviki/doku.pf?id=belong:msms

may be improved by repeating the TLC using different solvents. The advantage of TLC, however, is that it is usually possible to separate and observe the different dyes. For example, a purple frame may be found to contain both a red and a blue dye.

Organic substances other than dyes can be analysed by a GC-MS analysis if they are sufficiently volatile. Therefore, a GC-MS screening was performed on the purchased spectacle frames to identify other relevant organic substances in the spectacle frames.

For both the TLC screening and GC-MS, it is important to ensure that as many of the contained (dye) substances as possible are determined, and it is therefore important to be able to dissolve the spectacle frames completely or partially. The choice of solvent will depend on the type of material used for the different spectacle frames. Therefore, an FT-IR screening (Fourier-Transform Infrared Spectroscopy) was performed on most of the purchased products to identify the material used and allow selection of a suitable solvent for the spectacles in question.

In agreement with the Danish Environmental Protection Agency, the following screening analyses were therefore carried out:

- FT-IR for identifying material in the spectacles
- TLC for identifying certain dyes in the spectacles
- GC-MS screening for identification of volatile organic compounds in the spectacles.

4.2 FT-IR for identification of the material in the spectacles

FT-IR (Fourier-Transform InfraRed Spectroscopy) screening was performed on a selection of the 19 spectacles purchased[12]. FT-IR uses infrared radiation and the ability of materials to absorb this radiation differently to identify materials. The resulting spectrum is compared with a library of spectra to obtain an identification of the material. Fillers and phthalates added to the material will normally also be identifiable if they are present in large quantities (expected > 10%), but there is a risk that excessive amounts of fillers will "interfere" with the spectrum of the base material, which may complicate the identification of the material. Phthalates can usually be identified if they are present in large quantities, but not necessarily which specific phthalate is present. Other additives in smaller quantities cannot be identified with FT-IR.

4.2.1 Results of FT-IR analyses

The results of the FT-IR analyses, i.e. which material the spectacles in question consist of, are presented in below TABLE 20. The table also shows the information that was described on the website, or we have received from the manufacturers regarding the spectacle material.

Only 16 of the 19 spectacle frames purchased were analysed using FT-IR. This is because several spectacle frames made of the same material, but in different colours. were received from one manufacturer, and a sample of only one colour was subjected to FT-IR analysis to identify the main material.

[12] Glasses no. 1 was not available in time to be sent before the analyses were initiated, and therefore a total of only 19 spectacle frames have been analyzed.

TABLE 20. Results of FT-IR analyses. Material identification of the purchased spectacles.

Product No.*	Frame colour	Material according to survey	Material according to FT-IR analysis
2	Tortoiseshell	Unknown	Nylon
3	Black	Recycled plastic	Nylon
4	Tortoiseshell	Acetate	Cellulose acetate, phthalate content
5	Black	Unknown	Polycarbonate
6	Tortoiseshell	Polycarbonate	Polycarbonate
7	Tortoiseshell	Prestige plastic	Maybe a co-polymer of styrene, acrylate and acrylamide
8	Tortoiseshell	Recycled plastic	Polyester
9	Black	Cellulose Propionate	Maybe a co-polymer of styrene, acrylate and acrylamide (same material as spectacles no. 7)
10	Tortoiseshell	Propionate	Cellulose Propionate
11	Black	Unknown	Cellulose acetate, phthalate content
12	Tortoiseshell	Unknown	Cellulose acetate, phthalate content
13	Tortoiseshell	Bio-based material	Cellulose acetate, not containing phthalate
14	Tortoiseshell	Nylon	Nylon
15	Red	Nylon	Nylon
16	Tortoiseshell	Acetate plates. Cellulose acetate butyrate with DEP	Cellulose acetate, phthalate content
17	Brown	Acetate plates. Cellulose acetate butyrate with DEP	Not made, same material as spectacles no. 16
18	Red	Acetate plates. Cellulose acetate butyrate with DEP	Not made, same material as spectacles no. 16
19	Black	Rubber, temple tips. EPDM	Not made, same material as spectacles no. 20
20	Brown	Rubber, temple tips. EPDM	EPDM with talc

* Spectacles no. 1 was not available in time to be sent before the analyses were initiated and have therefore not been analysed.

4.3 Sample preparation for GC-MS and TLC

The FT-IR screenings showed that the 19 spectacles contain a total of six different materials (cellulose propionate and cellulose acetate are similar). In relation to the GC-MS and TLC screening, it is optimal that the spectacle material is ground (pulverised) so that it can be extracted most efficiently or dissolved in the appropriate solvent for the relevant material. The appropriate solvent and method must be chosen, partly in relation to the dissolution of the spectacle material and partly in relation to not destroying the dye so that it cannot be identified by the TLC screening.

However, the grinding of the spectacle frames was not entirely unproblematic. Several frames contained a metal wire in the temples that could not be immediately pulverized with a grinder. For the screening analyses, spectacle material was therefore chosen from other places on the spectacle where the metal wire was not present. Frame material without metal wire was ground as far as possible in a grinder with liquid nitrogen cooling. It was not possible to grind

all the materials completely to powders. Instead, some materials were ground into small grains (this was the case for e.g. EPDM rubber), or partially ground, where a little was powdered and the rest remained in larger pieces. Nylon could not be ground at all and was cut into small flakes, which were then dissolved or extracted.

A total of five different solvents were investigated for dissolving the different materials: THF (tetrahydrofuran), dichloromethane, acetone, ethyl acetate and methanol. Several solvents were tested for each material to determine the best functioning solvent, both in relation to dyes and GC-MS. Preferably, it should be possible to extract the dyes into the solvent, but at the same time it should be possible to use the resulting solution for the analysis, which was not possible, for example, if the solution became too viscous. For GC-MS, it should be possible to completely or partly dissolve the plastic in the solvent, in order to be able to identify as many substances as possible.

The following solvents were used for the final TLC screenings:
- THF (tetrahydrofuran) for full or partial dissolution of cellulose acetate/propionate, polycarbonate, the copolymer of styrene, etc. and polyester.
- Dichloromethane for the full or partial dissolution of cellulose acetate/propionate. Dichloromethane also dissolved polycarbonate, the copolymer of styrene, etc., and polyester in whole or in part.
- Acetone for dissolving cellulose acetate/propionate.
- Ethyl acetate for dissolving cellulose acetate/propionate.

Neither nylon nor EPDM (rubber) could be dissolved in the chosen solvents and therefore these materials were extracted with THF instead. Methanol could not dissolve any of the materials and was only able to extract small amounts of the dyes from the materials. Therefore, methanol was not used for the TLC screening. However, the methanol extracts were used for GC-MS (see below). Likewise, THF extracts or solutions of all spectacle frames were used for GC-MS.

The solutions/extracts for the TLC screening were prepared as concentrated as possible. Thus, 2-300 mg sample was added to 1.2 ml solvent and shaken for a minimum of 3 hours. Two different mobile phase solvents/eluents were used separately: acetone/heptane and ethyl acetate/heptane, to facilitate identification of the dyes. Solutions/extracts of the individual frames were first examined separately and compared with TLCs of the reference substances. Subsequently, samples where a possible content of a dye was identified were analysed together with the dye in question (co-spotted[13]).

4.4 TLC for identifying certain dyes

Based on the survey results, it was decided to purchase a total of nine dyes as reference substances (see TABLE 21). The dyes were selected on the basis of identification in the survey as used in plastic in general or in plastic frames, as well as on the basis of their problematic properties (primarily allergenicity).

[13] That is, when the sample and the reference substance are analyzed together (TLC spots separately and on top of each other) to see if the two substances are similar on the TLC plate, i.e. travel the same distance and thus are the same substance, or if they travel into two spots and thus show that the substances are different.

TABLE 21. Purchased reference dyes for detection via TLC

Dye	CAS No.	Reason for selection
Solvent Orange 60	6925-69-5	Notified classification: Skin Sens. 1B Seen allergic reactions from contact with spectacle frames
Solvent Yellow 14/ Sudan I	842-07-9	Harmonised classification: Skin Sens. 1 Seen allergic reactions from contact with spectacle frames
Solvent Red 179	6829-22-7	Classification according to REACH registration: Skin Sens. 1B Seen allergic reactions from contact with spectacle frames
Disperse Orange 3	730-40-5	Notified classification: Skin Sens. 1 Seen allergic reactions from contact with spectacle frames
C.I. Solvent Yellow 1 / 4-aminoazobenzene	60-09-3	Harmonised classification: Carc. 1B Notified Rating: Skin Sens. 1 Seen allergic reactions from contact with spectacle frames
PPD / p-Phenylenediamine	106-50-3	Harmonized classification: Skin Sens. 1, Acute Tox. 3 Seen allergic reactions from contact with spectacle frames
Disperse Yellow 3	2832-40-8	Harmonized classification: Skin Sens. 1, Carc. 2 Seen allergic reactions from contact with spectacle frames
Disperse Red 17	3179-89-3	Notified classification: Skin Sens. 1 Seen allergic reactions from contact with spectacle frames
Disperse Red 1	2872-52-8	Notified classification: Skin Sens. 1 Seen allergic reactions from contact with spectacle frames

TLC was performed on the dissolved or partially dissolved spectacle frame materials in the various solvents used, to detect whether one or more of the above reference dyes appear to be present in the 19 purchased spectacles. The results are listed on the next page.

Despite the use of concentrated solutions/extracts, the general picture from the TLC screening analyses was that the colours were weak and thus not easy to detect. Especially in spectacle frames with tortoise colours, many different colours were identified that were very close to each other or, in the worst case, on top of each other, which made detection more difficult. The dyes Solvent Orange 60 and Solvent Red 179 proved difficult to separate using TLC. In addition, several samples contained large amounts of a UV-active substance that ran together with Solvent Orange 60 and Solvent Red 179 and interfered with the image on TLC. In several cases, it is therefore difficult to assess whether a sample contained either one or the other dye in the sample - or neither or both.

As seen in TABLE 22 none of the colourants: PPD, Disperse Yellow 3 or Disperse Red 17 were detected in any of the 19 spectacle frames. The dyes Disperse Orange 3 and Disperse Red 1 were both seen in the same spectacle frame (no. 18), but the detection is rather uncertain and may thus originate from other colourants.

The dyes Solvent Yellow 14 and CI Solvent Yellow 1 were each detected in a single spectacle frame: in sample no. 5 and sample no. 17, respectively. These detections are marked in brackets, which means that these identifications are uncertain, but that these dyes may be in the samples.

TABLE 22. Results of the TLC screening analyses performed

Sample no.	Solvent used for TLC	Solvent Orange 60	Solvent yellow 14	Solvent Red 179	Disperse Orange 3	CI Solvent Yellow 1	PPD	Disperse Yellow 3	Disperse Red 17	Disperse Red 1	Comment
2	THF	(+) Very weak*		(+) Very weak*							Many coloured bands, all very weak
3	THF										
4	EtOAc										
5	THF	(+) uncertain	(+) uncertain								Many bands
6	THF			(+) Very weak							
7	THF	(+) uncertain*		(+) Very weak*							
8	THF										
9	THF										
10	THF	+									Further dilution of sample required for the use of TLC
11	Acetone	(+) uncertain*		(+) uncertain*							
12	EtOAc	(+) uncertain									
13	Acetone										
14	THF	+									
15	THF										
16	DCM	(+) uncertain									
17	DCM					(+) uncertain					
18	THF				(+) uncertain					(+) uncertain	
19	THF										
20	THF										

Abbreviations for the solvents used: THF = tetrahydrofuran, EtOAc = ethyl acetate, DCM = dichloromethane.

(+) means that the dye may be present in the sample – it is not a certain detection. The difference between "(+) very weak" and "(+) uncertain" should be understood in the sense that in the first case the detection is doubtful due to a very weak colour, whereas "(+) uncertain" means that the identification is uncertain, as many bands are on top of each other.

* The dyes Solvent Orange 60 and Solvent Red 179 are difficult to separate on TLC. It is therefore likely that there is either one or the other dye in the sample - or none or both.

As mentioned, the dyes Solvent Orange 60 and Solvent Red 179 proved to be difficult to separate on TLC. Solvent Red 179 may be found in three tortoiseshell frames (nos. 2, 6 and 7), but here the colour was very weak, and the identification was uncertain. In addition, Solvent Red 179 may be in a black frame (no. 11). In general, however, there is uncertainty as to whether it is the dye Solvent Red 179, Solvent Orange 60 or another third dye.

The dye Solvent Orange 60 appears to be the dye that has been detected in the most of the 19 examined spectacle frames. Solvent Orange 60 has been detected with reasonable certainty in samples no. 10 and 14, and may be present in samples no. 5, 12 and 16. In addition, it may also be that the dye occurs in samples 2, 7 and 11, but here it is more uncertain whether it is Solvent Orange 60, Solvent Red 179 or a completely third dye. Solvent Orange 60 was also identified in several spectacle frames using GC-MS (see section below).

4.5 GC-MS Screening for Organic Substances

For the GC-MS screening, two runs using two different solvents (one polar and one non-polar) were generally carried out in order to be able to identify as many different organic substances as possible. The two solvents used were THF and methanol. The spectacle frames could not be dissolved in methanol, which is why in practice it was extractions in methanol that have been made. For THF, some of the spectacle materials were dissolved in THF, while for other materials it is only an extraction (applies to EPDM rubber and nylon). The methanol extracts were prepared by adding 2-300 mg of sample to 1.2 mL of methanol, shaken for 3 hours, an internal standard was added and the extract was analysed directly. The THF solutions were prepared by adding 2 ml of THF to 2-300 mg of sample. The solutions were shaken for 3 h, then 4 mL of pentane was added to precipitate the polymer, filtered, an internal standard was added, and the sample was analysed with GC-MS. As far as possible, fully or partially ground samples were used for the THF samples.

At least the five largest peaks in the chromatograms for each sample have been identified using the NIST library (National Institute of Standards and Technology). In TABLE 23 below, the identified substances are marked in bold when their area is among the largest areas in the individual chromatogram (methanol extract, THF sample, or both). A number of the largest peaks in each sample have not been unambiguously identified and have therefore not been reported. Some of these unidentified substances could be various antioxidants that are added to the materials. The overall finding of the GC-MS screening has been reported, i.e. using both solvents (THF and methanol). In general, it is seen that the same eyewear materials often have the same additives added, e.g. antioxidants, UV stabilizers, or groups of substances that are clearly repeated in several samples (but which could not be identified). In several of the spectacles, methylated free fatty acids (so-called FAME) have also been identified, for the most part, in the methanol extract. In this case, it is possible that the materials contain e.g. plant oils or the free fatty acids, and that the presence of methylated free fatty acids in the methanol extract is due to them being formed during the extraction.

Below organic substances that have been identified in each individual spectacle material for the 19 analysed spectacle frames are presented. In TABLE 24 in the prioritisation section, on the other hand, shows the individual substances that have been identified, as well as which spectacle samples they were identified in. In TABLE 23, the quantity of the substances identified in relation to the content of the internal standard in the sample is indicated by one to four '+' symbols. Four + symbols are given for e.g. the identified phthalates, where the content is probably a few percent. The indication of the amount using + symbols is probably roughly equivalent to the content concentrations below. However, these are only estimated amounts, as the amounts are calculated relative to the internal standards, not the individual substance, and as the measured content in the extracts is affected by how efficiently the individual substance is extracted from the plastic. Since there is a difference in how the methanol and the THF samples were produced, e.g. in relation to the ratio between the amount of plastic used

and the amount of solvent used, and as there is a difference in the polarity of the solvents used, several cases showed large differences in the chromatograms between the estimated amount based on the THF sample and the estimated amount based on the methanol sample. The tables below indicate the maximum estimated content concentration.

(+) denotes a substance where the identification is correct, but the content is very low and the presence of the substance is therefore uncertain
+ corresponds to an estimated content of less than 60 ppm
++ corresponds to an estimated content of 60-600 ppm
+++ corresponds to an estimated content of 600-6000 ppm or 0.06-0.6%
++++ corresponds to a content of 6000 ppm or more – for phthalates in many cases a few percent

The EU harmonised human hazard classification of the substances is given in a separate column (Annex VI to the CLP Regulation), in order to assess whether this can provide a basis for prioritisation for quantitative analyses.

TABLE 23. Organic substances identified by a GC-MS screening in the 19 different purchased spectacle frames

Sample no.	Name of identified substance	CAS No.	Approximate quantity	Annex VI to CLP
2	**DEP (diethylphthalate)**	**84-66-2**	**++**	-
	1-butyl-2-pyrrolidinone	**3470-98-2**	**++**	-
	dimethyl ester hexanedioic acid**	627-93-0	+	-
	dimethylglutarate**	1119-40-0	+	-
	dimethylphthalate*	131-11-3	+	-
	2,6-di-tert-butyl-p-cresol (BHT)	128-37-0	+	-
	dimethylsuccinate**	106-65-0	+	-
	methyloctanoate**	111-11-5	+	-
	methylpalmitate**	112-39-0	+	-
	methylstearate**	112-61-8	+	-
	Solvent Orange 60	6925-69-5	(+)	-
	2-butoxyethylacetate	112-07-2	(+)	Acute Tox. 4 H312, H332
	2,4-di-tert-butylphenol	96-76-4	+	Acute Tox. 4 H302, Skin Sens. 1B H317, STOT RE 2 H373 Repr. 1B H360D
3	**caprolactam**	**105-60-2**	**++**	**Acute Tox. 4 H302, Skin Irrit. 2 H315**
	2-butoxyethylacetate	**112-07-2**	**++**	**Acute Tox. 4 H312, H332**
	triethyl citrate	77-93-0	+	-
	1-methoxy-2-propyl acetate***	**108-65-6**	**+**	**Flam. Liquid 3 H226**
	methyloctanoate**	111-11-5	+	-
	methylpalmitate**	112-39-0	+	-
	methylstearate**	112-61-8	+	-
	DEP (diethylphthalate)***	84-66-2	+	-
	2,4-di-tert-butylphenol	96-76-4	+	Acute Tox. 4 H302,

Sample no.	Name of identified substance	CAS No.	Approxi-mate quan-tity	Annex VI to CLP
				Skin Sens. 1B H317, STOT RE 2 H373 Repr. 1B H360D
4	**DEP (diethylphthalate)**	**84-66-2**	**++++**	-
	methylethylphthalate**	**34006-77-4**	**+++**	-
	dimethylphthalate*	131-11-3	++	-
	drometrizole (UV Absorber P)	2440-22-4	++	-
	o-acetyltriethyl citrate	77-89-4	+	-
	2-ethyl-1-hexanol	104-76-7	+	-
	2-ethylhexylstearate	22047-49-0	+	-
	5,5-dimethyl-2-phenoxy-1,3,2-dioxaphos-phorinane 2-oxide	884-89-9	+	-
5	**DEP (diethylphthalate)**	**84-66-2**	**+**	-
	dimethylglutarate**	**1119-40-0**	**+**	-
	dimethyl ester hexanedioic acid**	**627-93-0**	**+**	-
	m-tert-butyl-phenol***	**585-34-2**	**++**	-
	octrizol (UV absorber)	**3147-75-9**	**++**	-
	methylethylphthalate**	34006-77-4	+	-
	dimethylphthalate*	131-11-3	+	-
	1-methoxy-2-propyl acetate***	**108-65-6**	**+**	**Flam. Liquid 3 H226**
	dimethylsuccinate**	**106-65-0**	**+**	-
	methyloctanoate**	111-11-5	+	-
	methylpalmitate**	112-39-0	+	-
	methylstearate	112-61-8	(+)	-
	Solvent Orange 60	6925-69-5	(+)	-
	phenol***	**108-95-2**	**++**	**Acute Tox. 3 H301, H311, H331** **Skin Corr. 1B H314** **Muta. 2 H341** **STOT RE 2 H373**
6	**methyllaurate****	**111-82-0**	**+**	-
	dimethyl ester hexanedioic acid**	**627-93-0**	**+**	-
	dimethylglutarate**	**1119-40-0**	**+**	-
	dimethylphthalate*	**131-11-3**	**+**	-
	DEP	84-66-2	+	-
	2,6-di-tert-butyl-p-cresol (BHT)	128-37-0	+	-
	butylpalmitate***	**111-06-8**	**++**	-
	dimethylsuccinate**	106-65-0	+	-
	methylbenzoate**	**93-58-3**	**+**	-
	methyloctanoate**	111-11-5	+	-
	bis(2-isopropyl-5-methylcyclo-hexyl)methylphosphonate****	998510-36-8/ 998510-36-7/ 998510-36-9	+	-
	phenol***	**108-95-2**	**++**	**Acute Tox. 3 H301, H311, H331** **Skin Corr. 1B H314** **Muta. 2 H341** **STOT RE 2 H373**
7	DEP***	84-66-2	+	-

Sample no.	Name of identified substance	CAS No.	Approxi-mate quan-tity	Annex VI to CLP
	dimethylglutarate**	**1119-40-0**	**++**	-
	dimethyl ester hexanedioic acid**	**627-93-0**	**++**	-
	methyllaurate**	**111-82-0**	**+**	-
	dimethylphthalate*	131-11-3	+	-
	butylpalmitate***	**111-06-8**	**++**	-
	1-methoxy-2-propyl acetate	**108-65-6**	**+**	**Flam. Liquid 3 H226**
	2,6-di-tert-butyl-p-cresol (BHT)	128-37-0	+	-
	dimethylsuccinate**	106-65-0	+	-
	methylbenzoate**	**93-58-3**	**+**	-
	methyloctanoate**	111-11-5	+	
	methylstearate**	112-61-8	(+)	-
	bis(2-isopropyl-5-methylcyclo-hexyl)methylphosphonate****	998510-36-8/ 998510-36-7/ 998510-36-9	+	-
	phenol***	108-95-2	+	Acute Tox. 3 H301, H311, H331 Skin Corr. 1B H314 Muta. 2 H341 STOT RE 2 H373
8	methyllaurate	111-82-0	++	-
	dimethylphthalate*	**131-11-3**	**+**	-
	2,4-dimethyl-3-pentanone	**565-80-0**	**+**	**Acute Tox. 4 H332**
	dimethyl ester hexanedioic acid**	627-93-0	+	-
	1-methoxy-2-propyl acetate***	108-65-6	+	Flam. Liquid 3 H226
	camphene***	**79-92-5**	**+**	-
	dicyclohexylmethylphosphonate***	**7040-53-1**	**++**	-
	methyllaurate**	**111-82-0**	**++**	-
	methylpalmitate**	112-39-0	+	-
	bis(2-isopropyl-5-methylcyclo-hexyl)methylphosphonate****	998510-36-8/ 998510-36-7/ 998510-36-9	+	-
9	**dimethylglutarate****	**1119-40-0**	**+**	-
	dimethyl ester hexanedioic acid**	**627-93-0**	**+**	-
	methyl-2-ethylhexanoate	**816-10-3**	**+**	-
	dimethylphthalate*	131-11-3	+	-
	DEP	84-66-2	+	-
	2,4-dimethyl-3-pentanone	**565-80-0**	**+**	**Acute Tox. 4 H332**
	2,6-di-tert-butyl-p-cresol (BHT)	128-37-0	+	-
	dicyclohexylmethylphosphonate***	**7040-53-1**	**++**	-
	methyl-3-(3,5-Di-tert-butyl-4-hydroxyphenyl)pro-pionate**	6386-38-5	+	-
	methyloctanoate**	111-11-5	+	-
	methylstearate**	112-61-8	(+)	-
	poly(ethylene glycol)-bis(2-ethylhexano-ate)***	**94-28-0**	**++**	-
	bis(2-isopropyl-5-methylcyclo-hexyl)methylphosphonate****	998510-36-8/ 998510-36-7/ 998510-36-9	+	-
10	**bis(2-ethylhexyl)adipate or dioctyladipate*****	**103-23-1 / 123-79-5**	**++++**	-

Sample no.	Name of identified substance	CAS No.	Approxi-mate quan-tity	Annex VI to CLP
	dimethylglutarate	1119-40-0	+++	-
	2-butoxyethylacetate	112-07-2	++	Acute Tox. 4 H312, H332
	octylmethyladipate or 2-isohexylmethyladipate**, ***	998324-52-5 / 998324-52-2	++	-
	dimethylsuccinate	106-65-0	++	-
	dimethylglutarate	**1119-40-0**	**+++**	-
	2,4-di-tert-butylphenol	**96-76-4**	**+++**	-
	DEP	84-66-2	+	-
	propanoic acid	79-09-4	+	Skin Corr. 1B H314
	dimethyl ester hexanedioic acid	627-93-0	++	-
	dimethylsuccinate	106-65-0	++	-
	n-butylacetate	123-86-4	++	STOT SE 3 H336
	2-ethyl-1-hexanol* **	**104-76-7**	**++**	-
	1-methoxy-2-propyl acetate***	108-65-6	+	Flam. Liquid 3 H226
	2-ethylhexylstearate	22047-49-0	+	-
	methylbenzoate**	93-58-3	+	-
	methylpalmitate**	112-39-0	+	-
	methylstearate**	112-61-8	++	-
	Solvent Orange 60	6925-69-5	+	-
	methyl-3-(3,5-Di-tert-butyl-4-hydroxyphenyl)pro-pionate**	6386-38-5	+	-
	phenol***	108-95-2	++	Acute Tox. 3 H301, H311, H331 Skin Corr. 1B H314 Muta. 2 H341 STOT RE 2 H373
11	**DEP**	**84-66-2**	**++++**	-
	***o*-acetyltriethyl citrate**	**77-89-4**	**++++**	-
	methylethylphthalate**	34006-77-4	++	-
	glycerol 1,2-diacetate***	102-62-5	++	-
	2-ethylhexylstearate	22047-49-0	++	-
	drometrizole	2440-22-4	++	-
	2-ethyl-1-hexanol	104-76-7	+	-
	Irganox 1076***	2082-79-3	+	-
	triethyl citrate	77-93-0	++	
	methyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)pro-pionate**	6386-38-5	+	-
	5,5-Dimethyl-2-phenoxy-1,3,2-dioxaphos-phorinane 2-oxide	884-89-9	+	-
12	**DEP**	**84-66-2**	**++++**	-
	ethyl lactate	**97-64-3**	**+++**	**STOT SE 3 H335 Eye Dam. 1H318**
	methylethylphthalate**	**34006-77-4**	**+++**	-
	dimethyl(p-methoxybenzyliden)malonate	7443-25-6	++	-
	glycerol 1,2-diacetate* **	**102-62-5**	**++**	-
	methyllactate**	547-64-8	+	STOT SE 3 H335 Eye Irrit. 2 H319
	dimethylphthalate*	131-11-3	+++	-
	dimethyl(p-methoxybenzylidene)	7443-25-6	++	-
	Solvent Orange 60	6925-69-5	+	-

Sample no.	Name of identified substance	CAS No.	Approxi-mate quan-tity	Annex VI to CLP
13	**o-acetyltriethyl citrate**	**77-89-4**	**++++**	-
	DEP	84-66-2	+++	-
	glycerol 1,2-diacetate***	102-62-5	++	-
	triethyl citrate	77-93-0	+++	-
	4-tert-amylphenol	80-46-6	++	-
	2-ethyl-1-hexanol	104-76-7	+	-
	2-ethylhexylstearate	22047-49-0	++	-
	drometrizole	2440-22-4	++	-
	methylpalmitate**	112-39-0	(+)	-
	bis(2-isopropyl-5-methylcyclo-hexyl)methylphosphonate****	998510-36-8/ 998510-36-7/ 998510-36-9	++	-
14	**dimethyl ester hexanedioic acid****	**627-93-0**	**++**	-
	dimethylglutarate**	**1119-40-0**	**++**	-
	2-butoxyethylacetate	**112-07-2**	**+**	**Acute Tox. 4 H312, H332**
	DEP	84-66-2	+	-
	dimethylphthalate*	131-11-3	+	-
	2,4-di-tert-butylphenol	96-76-4	+	-
	2,6-di-tert-butyl-p-cresol (BHT)	128-37-0	+	-
	dimethylsuccinate**	106-65-0	+	-
	methyloctanoate**	111-11-5	+	-
	methylpalmitate**	112-39-0	+	-
	methylstearate**	112-61-8	+	-
	Solvent Orange 60	6925-69-5	+	-
	methyl-3-(3,5-di-tert-butyl-4-hydroxy-phenyl)propionate**	**6386-38-5**	**+**	-
	bis(2-isopropyl-5-methylcyclo-hexyl)methylphosphonate****	**998510-36-8/ 998510-36-7/ 998510-36-9**	**++**	-
15	2,4-di-tert-butylphenol	96-76-4	+	-
	methylpalmitate**	**112-39-0**	**(+)**	-
	methylstearate**	**112-61-8**	**+**	-
	bis(2-isopropyl-5-methylcyclo-hexyl)methylphosphonate****	**998510-36-8/ 998510-36-7/ 998510-36-9**	**+**	-

Sample no.	Name of identified substance	CAS No.	Approxi-mate quan-tity	Annex VI to CLP
16	**DEP**	**84-66-2**	**++++**	-
	glycerol 1,2-diacetate* **	**102-62-5**	**+++**	-
	ethyl lactate	**97-64-3**	**+++**	**STOT SE 3 H335 Eye Dam. 1H318**
	methylethylphthalate**	**34006-77-4**	**+++**	-
	dimethyl(p-methoxybenzyliden)malonate	**7443-25-6**	**+++**	-
	dimethylphthalate	**131-11-3**	**+++**	-
	methyllactate**	547-64-8	++	STOT SE 3 H335 Eye Irrit. 2 H319
	ethylisopropylphthalate***	998314-99-6	+	-
	methylpalmitate**	112-39-0	+	-
	o-acetyltriethyl citrate	77-89-4	++	-
	Solvent Orange 60	6925-69-5	+	-
	bis(2-isopropyl-5-methylcyclo-hexyl)methylphosphonate****	998510-36-8/ 998510-36-7/ 998510-36-9	++	-
17	**DEP**	**84-66-2**	**++++**	-
	methylethylphthalate**	**34006-77-4**	**+++**	-
	dimethylphthalate	**131-11-3**	**+++**	-
	4-tert-amylphenol	80-46-6	++	-
	2-ethyl-1-hexanol	104-76-7	+	-
	2-ethylhexylstearate	22047-49-0	++	-
	drometrizole	2440-22-4	++	-
	methyloctanoate**	111-11-5	+	-
	methylpalmitate**	112-39-0	(+)	-
	p-octylacetophenone	**10541-56-7**	**++**	-
	methyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)pro-pionate**	6386-38-5	+	-
18	**DEP**	**84-66-2**	**++++**	-
	methylethylphthalate	**34006-77-4**	**+++**	-
	dimethylphthalate	**131-11-3**	**+++**	-
	drometrizole	2440-22-4	++	-
	2-ethyl-1-hexanol	104-76-7	+	-
	2-ethylhexylstearate	22047-49-0	++	-
	4-tert-amylphenol	80-46-6	(+)	-
	methylpalmitate**	112-39-0	(+)	-
	methylstearate**	112-61-8	(+)	-
	methyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)pro-pionate**	6386-38-5	++	-
19	**methylstearate**	**112-61-8**	**++**	-
	methylpalmitate	**112-39-0**	**++**	-
	Irganox 1076***	**2082-79-3**	**+++**	-
	DEP	**84-66-2**	**++**	-
	tris(2,4-di-tert-butylphenyl)phosphite	31570-04-4	++	-
	2,4-di-tert-butylphenol	96-76-4	+	-
	2-butyl-1-octanol	3913-02-8	+	-
	heptadecanoic acid methylester	1731-92-6	+	-
	methylarachidate**	1120-28-1	+	-
	methylethylphthalate**	34006-77-4	+	-
	methylpalmitate**	112-39-0	++	-

Sample no.	Name of identified substance	CAS No.	Approxi-mate quan-tity	Annex VI to CLP
	methylstearate**	112-61-8	++	-
	methyltetradecanoate**	124-10-7	+	-
	p-octylacetophenone	**10541-56-7**	**+**	-
	methyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)pro-pionate**	6386-38-5	++	-
	bis(2-isopropyl-5-methylcyclo-hexyl)methylphosphonate****	998510-36-8/ 998510-36-7/ 998510-36-9	+	-
20	**DEP**	**84-66-2**	**++**	-
	2,4-di-tert-butylphenol	**96-76-4**	**+**	-
	methylstearate	112-61-8	+	-
	methylethylphthalate**	34006-77-4	+	-
	methylpalmitate**	112-39-0	+	-
	methylstearate**	112-61-8	+	-
	p-octylacetophenon3,5-di-tert-butyl-4-hy-droxybenzaldehyde	**10541-56-7** **1620-98-0**	**++** **+**	- -
	methyl-3-(3,5-di-tert-butyl-4-hydroxy-phenyl)propionate	**6386-38-5**	**++**	-
	bis(2-isopropyl-5-methylcyclo-hexyl)methylphosphonate	998510-36-8/ 998510-36-7/ 998510-36-9	+	-
	2,4,6-tri-tert-butylphenol	**732-26-3**	**+**	**Acute Tox. 4 H302, Skin Sens. 1B H317, STOT RE 2 H373 Repr. 1B H360D**

Bold indicates that the signal for the substance is among the most intense signals in the sample. Either in the methanol extract, the THF solution, or in both.

* Note that for dimethyl phthalate, this phthalate, except for samples no. 16, 17 and 18, is only identified in the methanol extract and not in THF and that the samples also contain large amounts of DEP. This could indicate that a re-esterification has occurred, i.e. DEP has reacted with methanol and formed dimethylphthalate. Often ethylmethylphthalate is also seen in the same samples, i.e. the half-reacted sample.

** These substances occur mainly or exclusively in the extract from methanol, but not in the extract from THF. The presence of the substance in the material is therefore uncertain, as it may be due to a reaction with methanol that it is present in the methanol extract.

*** The identification of the substance is uncertain.

**** The sample contains four signals that are consistently identified as one of the three isomers of this substance. The four signals are seen in several different samples, each time in approximately the same proportion, and are thus expected to originate from the same additive.

Several phthalates have been identified in the different spectacle frames. There are only a few frames without phthalate content. The phthalate DEP has been identified in the majority (17) of the 19 examined spectacle frames and has been identified in relatively high amounts in some of the spectacle frames (marked with ++++ corresponding to a content of a few percent). In a handful of the spectacle frames, it appears that the DEP content may be around 10% or more.

Dimethyl phthalate has also been identified in a large number of the examined spectacle frames, but in most of the cases dimethyl phthalate has only been identified in the methanol extract, but not in THF, which could indicate that a re-esterification has taken place, i.e. DEP has reacted with methanol and formed dimethyl phthalate. It is therefore possible that dimethyl phthalate is actually only found in three products.

Methyl ethyl phthalate has been identified in nine of the 19 products, but is also primarily seen in the methanol extracts, except for sample 18, and is mainly seen when the sample contains large amounts of DEP.

Solvent Orange 60 has been identified in small concentrations in some of the analysed spectacle frames, although GC-MS is not the right method of analysis for this dye. Solvent Orange 60 has been identified in spectacles no. 2, 5, 10, 12, 14 and 16, thus confirming the results of the TLC analyses in these spectacle frames.

Of the substances identified in the GC-MS screening, only a few of the substances have an EU-harmonised classification (see TABLE 23). Of substances with a harmonised classification, it can be noted that only a few of these classifications include special properties of concern such as CMR effects and sensitising effects. These substances are phenol (Muta. 2), 2,4,6-tri-tert-butylphenol (Repr. 1B and Skin Sens. 1B) and BHT (the only harmonised classification is environmental, but it is a suspected endocrine disruptor). These substances have in common that they are identified at very low levels (+), although phenol is at a slightly higher level (++), but the identification of phenol is uncertain, as the background in the chromatograms interferes with the phenolic signal and possibly contributes to the area of the peaks, which makes any phenol content appear greater.

As indicated earlier, not all substances could be identified by the GC-MS screening. There are quite a few larger peaks, which seem to be various antioxidants or UV stabilizers, or something else. For example, several spectacle frames with the same materials contain groups of additives that could not be identified, but which are repeated in the samples.

4.6 Prioritisation of substances for migration analyses

TABLE 24 below shows selected substances identified by the screening analyses in the 19 different spectacle frames. Only substances that may have been detected in the TLC screening or that have been identified in more than one spectacle frame, have a harmonised classification or are identified in high concentrations are listed in TABLE 24 below. That is, substances without classification and identified in low concentrations are not shown in the table below, even though they are identified in many spectacle frames. It is stated in how many products the substances have been detected, as well as in which of the products. This information is linked with the classification of the substances.

As not many of the substances have a harmonised classification, the classification according to the REACH classification dossier has also been examined for all substances (but not reported for all) and has been included in relation to the choice of prioritisation of substances for the subsequent migration analyses.

TABLE 24. Overview of detected substances in the 19 analysed spectacle frames

Substance name	CAS No.	Detected in x out of 19 frames	Detected in spectacle frame no.	Max. ca. concentration.	Classification[1]
Colouring					
Solvent Orange 60	6925-69-5	6 (8)	With TLC: 10 and 14, possibly also in 2, 5, 7, 11, 12, 16 With GC-MS in 10, 12, 14 and 16, possibly in 2 and 5	-	-
Solvent Yellow 14	842-07-9	1	5	-	**Carc. 2 H352** **Muta. 2 H341** **Skin Sens. 1 H317**
Solvent Red 179	6829-22-7	1 (4)	11 Possibly also in 2, 6 and 7	-	-
CI Solvent Yellow 1	60-09-3	1	17	-	**Carc. 1B H350**
Disperse Orange 3	730-40-5	1, but uncertain	18	-	-
Disperse Red 1	2872-52-8	1, but uncertain	18	-	-
Volatile substances					
Glycerol 1,2-diacetate***	102-62-5	4, but uncertain	11, 12, 13 and 16	+++	-
2-Ethyl-1-hexanol	104-76-7	6	4, 10, 11, 13, 17, 18	++	Skin Irrit. 2 H315; Eye Irrit. 2 H319; Acute Tox. 4 H332; STOT SE 3 H335
Caprolactam	105-60-2	1	3	++	**Acute Tox. 4 H302, H332; Skin Irrit. 2 H315; Eye Irrit. 2 H319; STOT SE 3 H335**
Dimethylsuccinate**	106-65-0	1 (6)	2, 5, 6, 7, 14 in methanol 10 in methanol and THF	++	-
1-Methoxy-2-propyl acetate	108-65-6	5	3, 5, 7, 8, 10	+	**Flam. Liq. 3 H226** STOT SE 3 H336
Phenol***	108-95-2	4, but uncertain	5, 6, 7 and 10	++	**Acute Tox. 3 H301, H311, H331; Skin Corr. 1B H314; Muta. 2 H341, STOT RE 2 H373**
Dimethylglutarate**	1119-40-0	1 (7)	2, 5, 6, 7, 9, 14 in methanol 10 in methanol and THF	+++	-
2-Butoxyethylacetate	112-07-2	4	2, 3, 10 and 14	++	**Acute Tox. 4 H312, H332**
n-Butylacetate	123-86-4	1	10	++	**STOT SE 3 H336**

Substance name	CAS No.	Detected in x out of 19 frames	Detected in spectacle frame no.	Max. ca. con-centration.	Classification[1]
2,6-Di-tert-butyl-p-cresol (BHT)	128-37-0	5	2, 6, 7, 9 and 14	+	-; Suspected endocrine disruptor
Dimethylphthalate*	131-11-3	3 (12)	16, 17 and 18 in methanol and THF 2, 4, 5, 6, 7, 8, 9, 12, 14 in methanol	+++	-
Drometrizole (UV Absorber P)	2440-22-4	5	4, 11, 13, 17 and 18	++	Skin Sens. 1 H317
Methylethylphthalate**	34006-77-4	1 (8)	4, 5, 11, 12, 16, 17, 19 in methanol 18 in methanol and THF	+++	-
1-Butyl-2-pyrrolidinone	3470-98-2	1	2	++	Acute Tox. 4 H302; Skin Irrit. 2 H315; Eye Irrit. 2 H319
Methyllactate**	547-64-8	(2)	12 and 16 in methanol	++	**Eye Irrit. 2 H319; STOT SE 3 H335**
2,4-Dimethylpentan-3-one	565-80-0	2	8 and 9	+	**Acute Tox. 4 H332** Uncertainty about REACH classification as Skin Sens. 1
Methyl-3-(3,5-di-tert-butyl-4-hydroxy-phenyl)propionate**	6386-38-5	(7)	9, 11, 14, 17, 18, 19, 20 in methanol	++	-
2,4,6-Tri-tert-butylphenol	732-26-3	1	20	+	**Acute Tox. 4 H302; Skin Sens. 1B H317; STOT RE 2 H373, Repr. 1B H360D**
o-Acetyltriethyl citrate	77-89-4	4	4, 11, 13 and 16	++++	-
Triethyl citrate	77-93-0	3	3, 11 and 13	+++	-
Propanoic acid	79-09-4	1	10	+	**Skin Corr. 1B H314**
4-Tert-amylphenol	80-46-6	2 (3)	13, 17, (18)	++	Skin Corr. 1B H314 Skin Sens. 1 H317 Eye Dam. 1 H318
DEP	84-66-2	17	2, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 14, 16, 17, 18, 19 and 20	++++	-
Methylbenzoate**	93-58-3	(3)	6, 7 and 10 in methanol	+	Acute Tox. 4 H302
2,4-Di-tert-butylphenol	96-76-4	7	2, 3, 10, 14, 15, 19 and 20	+++	Skin Irrit. 2 H315; Eye Dam. 1 H318
Ethyl lactate	97-64-3	2	12 and 16	+++	**Eye Dam. 1 H318; STOT SE 3 H335**
Octylmethyladipate or 2-isohexylmethyl-adipate***	998324-52-5 / 998324-52-2	1	10	++	-

1. Harmonised classification is indicated in **bold**. Classifications in normal print are classifications according to the REACH registration dossier.

* Note that for dimethylphthalate, this phthalate, except for samples no. 16, 17 and 18, is only identified in the methanol extract and not in THF and that the samples also contain large amounts of DEP. This could indicate that a re-esterification has occurred, i.e. DEP has reacted with methanol and formed dimethylphthalate. Often ethylmethylphthalate is also seen in the same samples, i.e. the half-reacted sample.

** These substances occur mainly or exclusively in the extract from methanol, but not in the extract from THF. The presence of the substance in the material is therefore uncertain, as it may be due to a reaction with methanol that it is present in the methanol extract.

*** The identification of the substance is uncertain.

**** The sample contains four signals that are consistently identified as one of the three isomers of this substance. The four signals are seen in several different samples, each time in approximately the same proportion, and are thus expected to originate from the same additive.

Based solely on the number of products in which the substances occur and in what quantities they occur in the screening analyses, the following substances should be prioritised:

Colouring:
- Solvent Orange 60
- Solvent Red 179
- Solvent Yellow 14 or
- CI Solvent Yellow 1

Organic volatiles:
- DEP (in 17 products in high quantities ++++)
- Methylethylphthalate (possibly in 8 products in higher quantities +++)*
- Dimethylphthalate (in 3 products in higher amounts +++)*
- Dimethylglutarate in seven products in higher amounts (+++)*
- Dimethyl ester hexanedioic acid in eight products in small quantities (++)*
- Methyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate in six products in small quantities (++)*
- 2,4-di-tert-butylphenol in four products in higher quantities (+++)
- 2,4-dimethylpentan-3-one in two products in smaller quantities (++), but there are uncertainties about a REACH classification as Skin Sens. 1
- Drometrizole in five products in smaller amounts (++), but REACH classification as Skin Sens. 1
- 4-tert-amylphenol in two products in smaller quantities (++), but REACH classification as Skin Sens. 1
- *o*-Acetyltriethyl citrate in four products in high quantities (++++)
- Triethyl citrate in three products in higher quantities (+++).

In samples marked with *, the content is uncertain, as the substance in the majority of spectacle frames only occurs in the extract from methanol, but not in the extract from THF. The content is therefore uncertain, as the presence of the substance may be due to methylation.

Only a few of the substances mentioned above have an EU-harmonised classification (see TABLE 24) and it can be noted that few of these classifications include properties of particular concern such as CMR effects and sensitising effect. A few substances (phenol, BHT and 2,4,6-tri-tert-butylphenol) have problematic properties, but are conversely identified only in a few products and in very low concentrations and are therefore not considered relevant for the subsequent migration analyses, partly because they are unlikely to be detectable in the migration fluid.

An overall assessment of the most important identified organic volatiles in relation to whether they should be prioritised for further analyses is presented below. The REACH classification and other information are taken into account in this prioritization.

The following criteria were used in the final prioritisation of substances from the screening analyses to the subsequent quantitative migration analyses:
- Number of spectacle frames where the substance is found
- Estimated maximum content amount, so that the substance is expected to be identifiable in a migration fluid
- Critical effect of the substance with focus on allergenic effects.

In addition, the final prioritisation for the subsequent migration analyses took into account whether migration analyses should be performed on dyes or organic volatiles, as these are two different analytical methods.

4.6.1 Overall hazard assessment and prioritisation of the most important substances from the GC-MS screening

The substances in the list above are assessed below for further prioritisation based on data found in the REACH registrations for the substances from the ECHA website: https://echa.europa.eu/en/home

DEP (Diethylphthalate, CAS 131-11-3): The substance is REACH registered in a tonnage band of 1000-10 000 tonnes per year, i.e. there are very extensive data requirements for the substance with regard to its hazards. The registration dossier concludes that no health hazard classifications are warranted and no dermal DNEL values are given due to the lack of toxic properties.

The substance has undergone the substance evaluation process under REACH and it has been concluded that there is no basis for hazard classification of the substance, and it is not considered that its use in consumer products poses a safety risk.

In 1991, a single case of allergy to DEP was reported, associated with the presence of the substance in spectacle frames. No further similar findings have been found in a literature search, and the National Allergy Research Centre does not consider it relevant to include the substance in a test package for ingredients in spectacle frames.

On this basis, it is not considered relevant to prioritise DEP for quantitative analysis and risk assessment.

DMP (Dimethylphthalate, CAS 131-11-3): The substance is REACH registered in a tonnage band of over 1000 tonnes per year, i.e. there are very extensive data requirements for the substance with regard to its hazards. There is only a little specific data on DMP in the registration dossier and most of the information has been determined by read-across from data on DEP. The substance has undergone the substance evaluation process under REACH, and the read-across approach has not been accepted as sufficient for the assessment of DMP's harmful effects on health and the environment. ECHA therefore requires a full dataset that meets the requirements for the current tonnage level.

On the basis of a lack of data, and since only one case of skin reaction to the spectacle frame (Crépy et al. 2011) has been reported, it is not considered relevant to prioritise DMP for quantitative analysis and risk assessment.

Methylethylphthalate (CAS 34006-77-4): The substance is not included in ECHA's substance database and is not a pre-registered substance, i.e. if the substance is produced, it is only to a very limited extent, and further searches on the Pubchem and Pubmed databases have not found toxicological data on the substance.

On the basis of a lack of data, it is not considered relevant to prioritise the substance for quantitative analysis and risk assessment.

Methyllaurate (CAS 111-82-0): The substance is REACH registered in the tonnage band 10 000-100 000 tonnes per year, so there are extensive data requirements for the substance. The registration dossier concludes that the data do not provide a basis for any health hazard classifications and no DNEL values are given due to the lack of toxic properties.

The substance has not been designated for further assessment in connection with the REACH processes.

Due to low toxicity, the substance is not considered relevant to prioritise for quantitative analysis and risk assessment.

Dimethylglutarate (CAS 1119-40-0): The substance is REACH registered in a tonnage band of 100-1000 tonnes per year, i.e. the data requirements for the substance regarding its hazardousness are at an intermediate level. The substance has undergone the substance evaluation process under REACH, and it has been concluded that there is no basis for hazard classification of the substance. Furthermore, the substance was assessed as non-problematic in terms of harmful endocrine disrupting effects.

The REACH registration dossier does not provide any dermal DNEL values due to lack of toxic properties.

Due to low toxicity, the substance is not considered relevant to prioritise for quantitative analysis and risk assessment.

Dimethyl ester hexanedioic acid, (dimethyl adipate), (CAS 627-93-0): The substance is REACH registered in the tonnage band 10 000–100 000 tonnes per year, so there are extensive data requirements for the substance. The registration dossier concludes that the data do not provide a basis for any health hazard classifications. The REACH registration dossier does not provide any dermal DNEL values due to lack of toxic properties.

The substance has undergone substance assessment under REACH, and ECHA has concluded that data for a number of health impact areas are insufficient and thus do not meet the data requirements.

Due to lack of data/low toxicity, the substance is not considered relevant to prioritise for quantitative analysis and risk assessment.

Methyl-3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate (CAS 6386-38-5): The substance is REACH-registered in a tonnage band of 1-10 tonnes per year, and therefore there are very few data requirements for the substance. The registration dossier concludes that the data do not provide a basis for any health hazard classifications. DNEL values have not been calculated for the substance. The REACH registration indicates that no data on skin sensitisation are available, but an OECD 421 study has been conducted (repeated dosing and screening for reproductive effects), where a NOAEL of 10 mg/kg bw/day is reported for maternal toxicity (effects on the liver at 100 and 250 mg/kg bw/day) and a NOAEL of 100 mg/kg bw/day for effects on reproduction (reduced survival of offspring at 250 mg/kg bw/day).

The substance has structural similarity with 4-tert-butylphenol, which is an SVHC substance due to endocrine disrupting effects in the environment, and ECHA (2021) has therefore listed the substance on a list of substances for which possible future regulation may be required.

At present, there is not considered to be a specific basis to prioritise the substance for quantitative analysis and risk assessment.

2,4-di-tert-butylphenol (CAS 96-76-4): The substance is REACH-registered in the tonnage band 1000–10 000 tonnes per year, so there are extensive data requirements for the substance. The registration dossier lists the health hazard classifications *Skin Irrit. 2 H315* and *Eye Dam. 1 H318*. In connection with substance assessment, the substance has been subject to several test requirements for both health and the environment in order to meet REACH data requirements, but the tests performed do not give rise to further health classification. The DNEL for skin contact is set at 6.25 mg/kg bw/day for workers, while it is not considered relevant to derive DNEL for the general population.

Due to its relatively low toxicity, the substance is not considered relevant to prioritise for quantitative analysis and risk assessment.

2,4-dimethylpentane-3-one (CAS 565-80-0): The substance is REACH-registered in the tonnage band 10–100 tonnes per year, so there are relatively few data requirements for the substance. In the registration dossier, the substance is classified with *Acute Tox. 4 H332*, which is also the EU-harmonised classification of the substance. A DNEL of 0.45 mg/kg bw/day has been reported for skin exposure of consumers based on a NOAEL value of 471 mg/m^3 in an OECD 421 rat study with inhalation exposure. The dossier states that 2 out of 3 different *in vitro* tests for skin sensitisation are positive, which is why the substance should be classified as skin sensitising. However, the substance is not given further priority for quantitative analysis and risk assessment due to the sparse data and as a result of the finding that the concentrations in spectacle frames are very low.

The following four substances are considered to be most relevant for quantitative analyses and risk assessment.

Drometrizole (CAS 2440-22-4): The substance is REACH registered in the tonnage band 1000–10,000 tonnes per year, so there are extensive data requirements for the substance. In the registration dossier, the substance has been classified with *Skin Sens 1B H317* on the basis of positive animal studies and a DNEL of 2.5 mg/kg bw/day has been indicated for dermal exposure. Based on skin sensitisation and the relatively high content in spectacle frames the substance is further prioritized for quantitative migration analysis and risk assessment.

4-tert-amylphenol (*p*-(1,1-dimethylpropyl)phenol, CAS 80-46-6): The substance is REACH registered in a tonnage band of 100-1000 tonnes per year, i.e. the data requirements for the substance with regard to its hazards are at an intermediate level. The substance has undergone the substance evaluation process under REACH, and it has been concluded that the substance is an SVHC substance due to endocrine disrupting effects in the environment. In the registration dossier, the substance has the following classifications for damage to health: *Skin Corr. 1B H314; Skin Sens. 1 H317, Eye Damage 1 H318.* In addition, a DNEL of 0.13 mg/kg bw/day has been given for skin exposure of consumers. Based on skin sensitisation and the relatively high content in the spectacle frames the substance is further prioritized for quantitative migration analysis and risk assessment.

***o*-acetyltriethyl citrate** (triethyl *o*-acetyl citrate, CAS 77-89-4): The substance is REACH registered in a tonnage band of 100-1000 tonnes per year, i.e. the data requirements for the hazards of the substance are at an intermediate level. The registration dossier does not classify the substance as a health hazard and no DNELs are given, but the dossier states that animal experimental data (from 1976) have demonstrated a strong sensitising effect. Due to the substance's potentially skin-sensitising properties and the relatively high content in the spectacle frames, the substance is prioritised for quantitative migration analysis and risk assessment.

Triethyl citrate (CAS 77-93-0): The substance is REACH registered in the tonnage band 1000–10 000 tonnes per year, so there are extensive data requirements for the substance. The registration dossier concludes that the data do not provide a basis for any health hazard classifications, but a DNEL of 12.5 mg/kg bw/day is indicated for skin exposure as regards systemic effects on consumers. In the dossier, it is stated that animal experimental data (from 1976) have demonstrated a strong sensitising effect. Due to the substance's potentially skin-sensitising properties and the relatively high content in the spectacle frames, the substance is prioritised for quantitative migration analysis and risk assessment.

4.6.2 Conclusion concerning prioritisation of substances for migration analyses

In cooperation with the Danish EPA it was decided to focus on organic substances identified in the screening analyses.

Four substances have been selected for quantitative migration analyses and risk assessment following a review of the organic substances found in the screening analyses, based on their occurrence in the spectacle frames, the estimated content concentrations and an initial assessment of the harmful properties of the substances:

- Drometrizole (CAS 2440-22-4)
- 4-tert-amylphenol (CAS 80-46-6)
- *o*-acetyltriethyl citrate (CAS 77-88-9)
- Triethyl citrate (CAS 77-93-0)

In the selection, particular emphasis has been placed on the skin sensitising effects.

For budgetary reasons, six spectacle frames were prioritised for quantitative migration analyses. The selected frames contained the highest expected amounts of one or more of the four substances above. Spectacle no. 3 was excluded despite detection of triethyl citrate as the content was considered to be low.

- Spectacles 4 – content of drometrizole and *o*-acetyltriethyl citrate
- Spectacles 11 – content of drometrizole, triethyl citrate and *o*-acetyltriethyl citrate
- Spectacles 13 – content of drometrizole and 4-tert-amylphenol and *o*-acetyltriethyl citrate and triethyl citrate
- Spectacles 16 – content of *o*-acetyltriethyl citrate
- Spectacles 17 – content of drometrizole and 4-tert-amylphenol
- Spectacles 18 – content of drometrizole and possible content of 4-tert-amylphenol

5. Migration analyses

As described in chapter 4.6, it was decided to select four substances for migration analysis due to the potential skin-sensitising properties of the substances for six of the purchased spectacle frames. The four substances and the six selected frames are listed in TABLE 25 below, where the colours in the table indicate which of the substances were identified in the individual spectacle frames during the screening analyses.

TABLE 25. Overview of the migration analyses performed. A coloured field indicates that the substance was identified during the screening analyses in the individual spectacle frames.

Spectacle frames	Drometrizole	4-tert-amylphenol	*o*-acetyltriethyl citrate	Triethyl citrate
Spectacles 4				
Spectacles 11				
Spectacles 13				
Spectacles 16				
Spectacles 17				
Spectacles 18		*		

* The screening only indicates a possible content of 4-tert-amylphenol in spectacles no. 18. The identification is not certain as the signal is close to the detection limit of the analysis method.

In this chapter, the method of analysis and the results of the migration analyses are described. For analytical reasons, the quantitative content of all four substances was measured in the migration fluid from all six spectacle frames, regardless of whether the substance was identified in the spectacle frames in question during the screening analysis or not.

5.1 Choice of migration fluid

Two migration fluids are typically selected for migration studies for medical devices that contact skin: an aqueous migration fluid with a relevant pH value and high ionic strength and a less polar migration fluid consisting of water and an organic solvent, typically an alcohol. The highest amounts of extracted metals are typically achieved in the aqueous migration fluid, while the other migration fluid extracts a wider range of organic substances in higher amounts.

Since the focus of this project is on the organic substances, a migration fluid containing water and alcohol is considered more relevant than the use of a very polar liquid with high ionic strength, such as artificial sweat. It should also be considered that in addition to sweat on the skin, the spectacle frames will also be in contact with fats from the skin as well as any oily skin lotion, each of which will promote the migration of non-polar organic substances from the spectacle frames. It is therefore proposed to use a migration fluid consisting of an ethanol:water mixture (1:1). This is a standard composition that is also used in migration analyses of food packaging. In addition, a migration duration of 72 hours is proposed at a temperature of 37°C. A migration duration of 72 hours is used, as the migration fluid has a longer time to affect the plastic material, which must be considered relevant as spectacles are worn daily and over a long period of time.

5.2 Method of analysis

A description of the sample preparation and the method of analysis used in the migration analyses is given below.

5.2.1 Sample preparation

The spectacle temples were used as the sample material for the migration analyses. However, for spectacles no. 16, 17 and 18, plates of spectacle material we received from the manufacturer, from which the spectacles had been cut, were used. In these cases, an oblong piece of the plates was cut out roughly corresponding to the height/width of a spectacle temple.

Pieces of temples/spectacle material of approximately 6 to 12 cm in length and approximately 3.5 to 6.5 mm in height and width were used. The total surface area was measured for all cut temples/spectacle materials and used to express the analysis results in µg of migrated substance per cm^2 surface area of the spectacle material. A whole temple or an equivalent piece of the spectacle material has been used for each individual determination.

Pieces of the spectacle material from products no. 16, 17 and 18 were cut into regular rectangular pieces and could thus be measured relatively precisely. The cut temples (products no. 4, 11 and 13) were measured by drawing the outline on paper, after which the surface area was calculated on the basis of the known density of the paper and weighing of the cut pieces of paper. It should be noted, however, that this calculation of the surface areas is subject to some degree of uncertainty. The uncertainty is estimated to be approximately 20-30%. The measured surface areas of the samples used for the migration analyses are given in TABLE 26 below.

TABLE 26. Measured surface area of samples used for the migration (average of duplicate determinations is indicated)

Spectables frames	Estimated area (cm^2)	Sample type
Spectables 4	18.7	Cut-off temple
Spectables 11	21.6	Cut-off temple
Spectables 13	16.0	Cut-off temple
Spectables 16	13.1	Cut sample from spectacle material
Spectables 17	13.0	Cut sample from spectacle material
Spectables 18	12.9	Cut sample from spectacle material

The spectacle temples used for samples 4, 11 and 13 each had a metal wire inside the plastic material. The metal wire has thus been in contact with the migration fluid at the cut surfaces in these cases.

Both the temple and the spectacle material were cut into an appropriate number of pieces (two to four pieces) so that the material could fit into a 10 ml vial and covered with a minimum of migration fluid. The number of pieces into which the spectacle material was cut was noted and used to calculate the surface area. Image of temples in sample glass and migration fluid can be seen in Figure 2.

5.2.2 Performance of migration tests and quality data of the analysis method

The cut pieces of spectacle material/temple were placed in a 10 ml vial and 8 ml of migration fluid (ethanol: water, mixed in a ratio of 1:1). Additional migration fluid was added in 0.5 ml increments if the initial amount of this liquid was not enough to cover the spectacle material, and the amount of fluid was noted.

The vials were closed and put in an incubator for 72 hours at 37 °C. At the end of the migration period, the samples were cooled, the temples removed and the migration liquid was transferred to a volumetric flask, a known amount of internal standard (benzyl alcohol) was added and the volumetric flask was filled to the mark. The migration fluid was filtered through a nylon filter and analysed using GC-MS. Samples with expected high content of one of the substances were diluted and both a concentrated and diluted sample were analysed.

The migration analyses were performed using genuine duplication of the analyses. In addition, five duplicate determinations were carried out for each of the controls (i.e. a total of 10 controls at low levels and 10 controls at high levels). The analyses included assessment of potential degradation of the substances during migration, evaluation of the linearity of the curve in the measurement range, measurement of the detection limits, etc. The detection limit in the migration fluid by the analytical method used is 1.8, 0.03, 0.12 and 0.12 µg/ml for the four substances drometrizole, 4-tert-amylphenol, *o*-acetyltriethyl citrate and triethyl citrate, respectively. The expanded uncertainty of the analysis was calculated to be 41, 35, 40 and 41 % for the four substances in the low control level (corresponding to approximately 10 µg substance/ml) and 20, 20, 33 and 20 % for the four substances in the high control level (corresponding to approximately 40 µg substance/ml). The recovery of controls with known concentrations that were treated in the same way as the samples and thus spent the same amount of time in the incubator as the samples was also analysed. The recoveries of the individual substances after 72 hours at 37 °C are as follows: 118, 93, 128 and 127% for the four substances drometrizole, 4-tert-amylphenol, *o*-acetyltriethyl citrate and triethyl citrate at the low control level and 112, 92, 107 and 101% for the four substances drometrizole, 4-tert-amylphenol, *o*-acetyltriethyl citrate and triethyl citrate at the high control level when calculated against the recovery of controls analysed directly (that have not been in the incubator).

During the GC-MS analysis, a degradation of the individual substances in the solution was observed, which gives rise to both higher uncertainties and poorer recovery of controls.

5.3 Results of the migration analyses

The results of the migration analyses are presented in TABLE 27 below. The results are given in the unit µg of substance per cm^2 of surface area of the spectacle material. The results show the amount of material that has migrated out of the frame material at 37 °C for 72 hours.

TABLE 27. Results of migration analyses. Values are generally given in µg/cm^2 of spectacle surface area, but note that for spectacles 11 and 13, the value of *o*-acetyltriethyl citrate is given in mg/cm^2 (in bold in the table), which is a factor of 1000 higher than for the other values

Spectacle frames	Drometrizole	4-tert-amylphenol	*o*-acetyltriethyl citrate	Triethyl citrate
Spectacles 4*	23 µg/cm^2	-	13 µg/cm^2	1.9 µg/cm^2
Spectacles 11*	24 µg/cm^2	-	**3.86 mg/cm^2**	44 µg/cm^2

Spectacle frames	Drometrizole	4-tert-amylphenol	*o*-acetyltriethyl citrate	Triethyl citrate
Spectacles 13*	27 µg/cm^2	0.01-0.04 µg/cm^2 **	**17.2 mg/cm^2**	357 µg/cm^2
Spectacles 16	-	-	42 µg/cm^2	2.5 µg/cm^2
Spectacles 17	32 µg/cm^2	5.0 µg/cm^2	4.8 µg/cm^2	0.4 µg/cm^2 ***
Spectacles 18	33 µg/cm^2	0.08 µg/cm^2	4.7 µg/cm^2	0.5 µg/cm^2 ***

- means that the substance has not been detected in the migration fluid for the listed spectacles.
* Due to greater uncertainty in determining the areas, there is a greater uncertainty in values.
** The content is below the limit of quantification but above the limit of detection.
*** Triethyl citrate content in samples 17 and 18 is only just above the limit of quantification

Two of the four substances were identified in the migration fluid but were not found in the screening analysis. These are the following substances:

- Triethyl citrate (identified in the migration fluid of spectacles 4, 16, 17 and 18)
- *o*-Acetyltriethyl citrate (identified in the migration fluid of spectacles 17 and 18)

The difference is due to the different conditions used for the screening analysis and the migration analysis. In the screening analysis, the material was extracted in an organic solvent for a relatively short time at room temperature, whereas the migration was carried out heated in an ethanol/water mixture for 72 hours. The difference in solvent, temperature and time can affect whether and how much a substance migrates. In addition, the instrumental part of the quantitative analysis method is designed to quantitatively measure the four selected substances in the migration fluids, whereas the screening method is designed to measure many different substances. The quantitative method is therefore more sensitive than the screening method.

In five out of six cases, the migration fluids were coloured, indicating quite clearly that the dyes identified in the screening analyses migrate out of the spectacle frames. Figure 2 below is a picture of the coloured migration fluids after pieces of temples/spectacle materials have been left in the migration fluid for 72 hours at 37 °C. The picture was taken immediately after the samples were taken out of the incubator.

Figure 1. Colours of migration fluids immediately prior to GC-MS analysis, i.e., after 72 hours at 37 °C.
The image shows from left to right the following samples: blind sample (colourless liquid), glasses 4 (pink liquid), spectacles 11 (dark blue liquid), spectacles 13 (colourless liquid), spectacles 16 (intense brown/orange liquid), spectacles 17 (weak light red liquid) and spectacles 18 (red liquid).

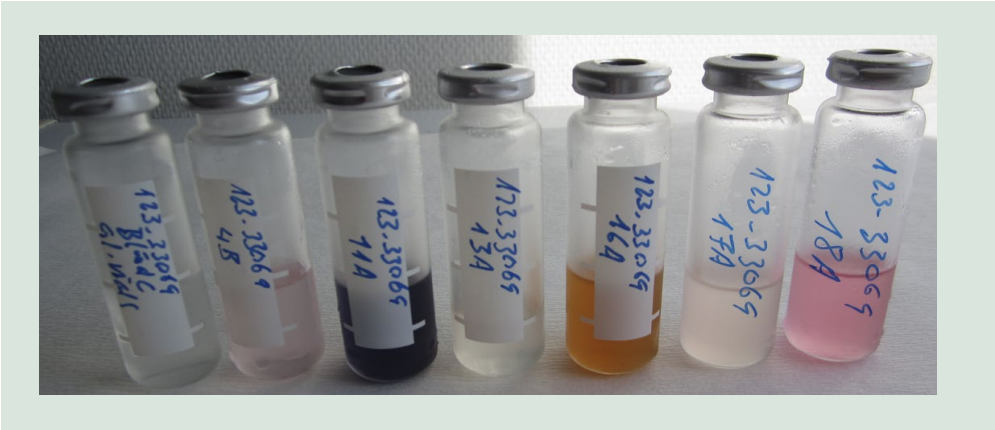


Figure 2. Colours of migration fluids after 72 hours and 37°C after being stored in the freezer.
The image shows from left to right the following samples: blank (colourless liquid), spectacles 4 (pink liquid), spectacles 11 (dark blue liquid), spectacles 13 (colourless liquid), spectacles 16 (strong brown/orange liquid), spectacles 17 (weak light red liquid) and spectacles 18 (light red liquid).

5.4 Discussion of the analysis results

When comparing TABLE 25 and TABLE 27 it can be seen that the four substances identified in the selected spectacles during the screening analyses are also found in the migration fluid from the six spectacles analysed, in all cases.

The substances drometrizole and *o*-acetyltriethyl citrate both migrate from five of the six selected spectacles, while triethyl citrate and 4-tert-amylphenol migrate from two and three of the six selected spectacles, respectively. The highest measured migration of the four substances is given below:

- Drometrizole migrates at highest concentration of 33 µg/cm^2 in spectacles 18
- 4-tert-amylphenol migrates at a peak concentration of 5.0 µg/cm^2 in spectacles 17
- *o*-acetyltriethyl citrate migrates at the highest concentration of 17.2 mg/cm^2 in spectacles 13 (note mg/cm^2 is a factor 1000 higher compared to the unit µg/cm^2)
- Triethyl citrate migrates at the highest concentration of 357 µg/cm^2 in spectacles 13

Triethyl citrate was identified in all six migration fluids. The substance *o*-acetyltriethyl citrate can be degraded to triethyl citrate via hydrolysis. The content of triethyl citrate relative to *o*-acetyltriethyl citrate in all six samples is approximately 10-100 times lower in the migration fluid, which suggests that there is a correlation between the concentrations of the two substances. This could be due to degradation, triethyl citrate occurring as an impurity in *o*-acetyltriethyl citrate or other reasons. This means that the identified content of triethyl citrate in the migration fluids does not necessarily reflect the actual content in the samples, as it may be due to degradation of *o*-acetyltriethyl citrate in the aqueous migration fluid.

It should be noted that only six migration analyses were carried out in total for budgetary reasons. As stated in section 4.5 (TABLE 24), the four selected substances were identified in five spectacles (drometrizole), three spectacles (4-tert-amylphenol), four spectacles (*o*-acetyltriethyl citrate) and three spectacles (triethyl citrate) respectively out of a total of 19 spectacles examined. No migration analysis was performed on spectacles no. 3, which according to the screening also contained (triethyl citrate). According to the screening analyses, the highest amount of triethyl citrate should be present in spectacle no. 13, the second highest in spectacle no. 11, and the lowest amount in spectacle no. 3 (for which no migration analysis has been performed). Since the highest migration of triethyl citrate occurs from spectacles no. 13 (with

the highest amount of content according to the screening), it is expected that the migration of triethyl citrate from spectacles no. 3 is lower than from spectacles no. 13. However, this has not been investigated and it should be noted that in the screening analyses, organic solvents were used for extraction and not ethanol/water as in the migration analyses.

All six spectacles examined in the migration analyses (spectacles no. 4, 11, 13, 16, 17 and 18) consist of the material cellulose acetate. Spectacles no. 4 are children's spectacles, while the remaining five examined spectacle materials are adult spectacles.

5.4.1 Discussion of coloured migration fluids

Figure 2 and Figure 3 clearly show that the colour from the temples penetrates into the migration fluid used. TABLE 28 below shows the colours identified in the screening analyses (using organic solvent as the extraction fluid) (TABLE 24) and the colours of the individual spectacle frames (TABLE 19) compared to the colours of the migration fluids (using ethanol/water as the migration fluid) (Figure 3). It should be noted that the colours in the liquids are an expression of all the dyes that migrate out of the spectacle material and not just the dyes that were the focus of the screening analyses.

TABLE 28. Colour of migration fluids compared to the colours of the spectacles and content of selected dyes identified by the screening analyses.

Spectacle frames	Colour of spectacle frames	Migration fluid colour	Identified selected dye by the screening analyses
4	Tortoiseshell	Light red liquid	*None of the dyes tested*
11	Black	Dark blue	Solvent orange 60 Solvent red 179
13	Tortoiseshell	Colourless	*None of the dyes tested*
16	Tortoiseshell	Brown/orange	Solvent Orange 60
17	Brown	Very light red liquid	CI Solvent Yellow 1
18	Red	Red	Disperse Orange 3 Disperse Red 1

It should be noted that the temples were cut for the migration analyses and several pieces of the temple were placed in the migration fluid. However, this is not expected to have a significant effect on migration as the temples selected were not expected to have been painted or otherwise surface treated. However, an uneven cut surface may have an effect on the degree of migration. This may have an impact on samples 16, 17 and 18 where samples were cut from sheets of spectacle material.

The amount of dyes that migrated was not measured in this project (the focus was on the four selected organic substances), but the colour of the migration fluids suggests that there may be significant migration of dyes from the spectacle frames. It should be noted that we did not investigate which dyes migrated in the migration fluid, only that several of the migration fluids were coloured after the temples were left in them for 72 hours at 37°C.

6. Hazard assessment

For the selected substances, a more in-depth hazard assessment is carried out, identifying relevant N(L)OAEL values for the critical effects of the substances and calculating dermal DNELs according to the REACH guidelines (ECHA 2012).

In the literature search for toxicological data, information for the substance was prioritised and searched for in the following order:

- Substance assessments from the EU's scientific committees e.g. SCHEER, SCCS, RAC, EFSA, etc.
- Substance assessments by other international and national expert committees, e.g. WHO, IPCS, IARC, US EPA, RIVM, BfR, etc.
- ECHA's data for the substances, including data from REACH registrations of the substances.
- Any previous assessment in the Danish Environmental Protection Agency's project reports.
- Any US FDA or EMA (EU Medicines Agency) data on the substances in connection with their use in medical devices.
- Web-based search on Google and PubMed.

Sensitising effects
In this project, there is a special focus on the local effects that can occur on the skin surface due to potential release of chemical substances from the spectacle frames. The critical effects are considered to be skin irritation and skin sensitisation. While there are guidelines for calculating DNELs for irritation, ECHA (2012) states that in practice it is very difficult to establish specific DNELs for skin sensitisation, as there are no well-established methods for this. A more qualitative approach is therefore often used to minimise the potential risk from sensitising substances where it is recommended to limit exposure to these substances as much as possible, rather than giving a specific quantitative target.

In recent years, however, a considerable amount of work has been done to achieve a quantitative assessment method for skin sensitisers. The most well-established of these methods, QRA2 (Quantitative Risk Assessment 2), has been developed by Api et al. (2008 + 2020) and further developed by Corea et al. (2023). In the latter, emphasis is placed on the use of EC3[14] values from LLNA (Local Lymph Node Assay) tests, which are a standardized skin sensitising test performed with mice (OECD TG 429 and OECD TG 442B).

The method for calculating an acceptable level of exposure (i.e. a DNEL) uses the following general steps:

- Setting a no effect level for induction of skin allergy (a so-called NESIL value - No Expected Sensitisation Induction Level)
- Application of Sensitisation Assessment Factors (SAFs)

I.e.

$$DNEL = NESIL / SAFs$$

[14] The EC3 value is the dose level having a three times higher response on the lymph nodes compared the response in the control animals (for more details see also the hazard assessment of 4-tert-amylphenol section 6.2).

The quantitative NESIL value (in µg/cm^2) is determined according to Api et al. (2008 + 2020) based on an expert assessment of the overall data, i.e. human data, *in vitro* and *in vivo* and *in silico* data.

Corea et al. (2023) describes the rationale for using the EC3 value from the LLNA test as the NESIL value, where the NESIL value for deriving the tolerable exposure level (the DNEL value) then is divided by a number of SAFs to take into account, among other things:

- SAF1: interspecies factor (set to 1 when using the LLNA EC3 value from LLNA mouse experiments (Corea et al. (2023), as data indicate overall compliance between EC3 values and human sensitisation thresholds.
- SAF2: for differences in sensitivity among the population a factor of 10 is used (Api et al 2020; (Corea et al. 2023)
- SAF3: frequency and duration of use of the product (set to 3 for long-term and repeated use (Api et al 2020)
- SAF4: The condition of the skin surface (set between 1 and 10 where, for example, increased values are used in connection with inflamed skin)
- Additional SAF can be used, for example, if the product's matrix is considered to enhance the induction of sensitising effects (SAF= 3) or if skin contact is of an indirect nature (SAF = 0.3).

In the hazard assessment of the substances, particular emphasis will therefore be placed on whether there is relevant human data or relevant LLNA test data for the substances, as this is considered the best starting point for determining NESIL and subsequent DNEL values for skin sensitisation.

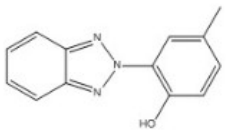
6.1 Drometrizole (CAS 2440-22-4)

6.1.1 General data

The substance is REACH registered in the tonnage band 1000 – 10 000 tonnes per year, so there are extensive data requirements for the substance. The substance is used for UV protection in a number of polymers and in surface treatment agents and in a number of consumer products, including cosmetics (Cosing 2024). In the registration dossier, the substance is classified with *Skin Sens 1B H317.*

TABLE 29 below lists the chemical identity and physicochemical data of the substance.

TABLE 29. Physicochemical data of Drometrizole (CAS 2440-22-4)

ID and physicochemical data		Reference
Chemical name	2-(2H-benzotriazol-2-yl)-p-cresol	REACH-reg. 2024a
Chemical structure		Health Canada 2021
Chemical Formula	$C_{13}H_{11}N_3O$	Health Canada 2021
Molecular weight	225 g/mol	Health Canada 2021
Melting point	130 °C	REACH-reg. 2024a
Boiling point	decomposes	REACH-reg. 2024a
Water solubility	0.173 mg/L at 20 °C	REACH-reg. 2024a
Log Pow	4.2 at 25 °C	REACH-reg. 2024a
Vapour pressure	1.47 x 10^{-4} Pa at 20 °C	REACH-reg. 2024a

6.1.2 Toxicological data

In addition to the REACH registration dossier, data searches have found the following relevant expert toxicological assessments of drometrizole:

CIR (2008). Amended Final Report of the Safety Assessment of Drometrizole as used in Cosmetics. International Journal of Toxicology, 27(Suppl. 1):63–75. Amended Final Report of the Safety Assessment of Drometrizole as used in Cosmetics1 (sagepub.com)

Health Canada (2021). Draft Screening Assessment Benzotriazoles and Benzothiazoles Group. Microsoft Word - 20210302-DSAR Benzotriazoles and benzothiazole-EN-published.docx (canada.ca)

Lee et al. (2019). Risk Assessment of Drometrizole, a Cosmetic Ingredient used as an Ultraviolet Light Absorber. Toxicol. Res. Vol. 35, No. 2, pp. 119-129 (2019). https://doi.org/10.5487/TR.2019.35.2.119

From the above references, the following key information can be summarised for the assessment of the toxicological properties of drometrizole.

Acute toxicity
The substance has low acute toxicity and LD50 values are significantly above the classification limit (REACH-reg 2024a; Lee et al 2019).

Irritation
Based on animal studies, the substance is not considered to be either skin or eye irritant (REACH-reg 2024a).

Sensitisation
The main study (key study) in the REACH dossier for assessing the sensitising effect of the substance is a skin allergy test performed with guinea pigs (GPMT, Guinea Pig Maximisation Test). In the study, 20 animals were induced on Day 1 with dermal injection of 0.1 mL of 5% drometrizole in peanut oil followed on day 2 with skin surface exposure of 30% drometrizole in petroleum. After 5 weeks, the animals were challenged with 20% drometrizole in petroleum jelly. One day and two days after the challenge, 16 and 18 of the 20 animals showed a positive skin sensitisation reaction, respectively. Based on this study, the substance was assigned a classification as Skin Sens 1B H317 (REACH-reg 2024a).

In another test performed as a precursor of the current LLNA test design, mice were given two injections into the skin of the abdomen with 25 µL of 0.2% drometrizole in olive oil, followed on days 5 to day 7 with daily dermal provocation exposures on the skin surface of the ears with 25 µl of varying concentrations of drometrizole. A 20% increase in ear thickness was observed following dermal exposure to 1% drometrizole, which was interpreted as a positive response.

In the original article for this study (Ikarshi et al 1994), a stimulation index (SI) of 15.1 was found for stimulation of the lymph nodes of the ears, which clearly supported the sensitising effect of the substance. A stimulation index of 3 (EC3) is currently used as a criterion for a positive sensitisation effect for an LLNA test, which, however, uses dermal exposure on the skin surface rather than dermal injection for the induction exposure.

Effects of repeated exposure.
In an oral OECD 422 rat study (combined reproduction and subacute study), NOAEL and LOAEL values of 30 mg/kg bw/day and 100 mg/kg bw/day, respectively, were found for the

parent generation for liver effects. No effects on foetal and newborn development were observed even at the highest dose of 300 mg/kg bw/day.

In a two-year feeding study in mice, no harmful effects were found at the highest dose of 62-64 mg/kg bw/day.

In a two-year feeding study in rats, reduced weight was found in rats at the highest dose of 142 mg/kg bw/day, and the NOAEL in the study was 47 mg/kg bw/day.
(REACH-reg2024a; Lee et al 2019).

In foetal development studies in mice and rats, dosing at 1000 mg/kg bw/day had no effect on foetal development (Lee et al 2019; REACH reg 2024a).

Mutagenic and carcinogenic effects
Drometrizole showed no mutagenic effects *in vitro*, either in bacterial strains or in mammalian cells. Mammalian cells examined for chromosomal abnormalities also showed no effect (REACH-reg 2024a).

In vivo studies in mice and hamsters produced no mutagenic/genotoxic effects at dose levels up to 2500 mg/kg bw and 2000 mg/kg bw, respectively (Lee et al 2019).

In the above mentioned 2-year feeding study with mice and rats at dose levels up to 64 mg/kg bw/day and 142 mg/kg bw/day, respectively, no increased tumour incidences were found in the animals.

Overall assessment and calculation of DNEL

Sensitisation
The substance has a sensitising effect, but with moderate potency, as the substance meets the CLP criteria for classification as Sens 1B H317. However, more accurate/updated data is required, such as an LLNA to assess the potency of the substance more accurately.

There are no specific quantitative data from which to derive a NESIL value, as data from the modified LLNA test are not considered sufficiently relevant due to the dosing method with intradermal injection rather than dermal application.

Systemic effects
The NOAEL of 47 mg/kg bw/day from a chronic feeding study in rats is considered a relevant starting point for calculating the DNEL value. As data are not available for oral or dermal absorption of the substance, the oral NOAEL value is used directly to calculate the dermal DNEL:

DNEL = NOAEL / (AF1 x AF2 x AF3)
DNEL = 47 mg/kg bw/day / 4 x 2.5 x 10
DNEL = 0.47 mg/kg bw/day.

where
AF1: is an uncertainty factor for extrapolation from animals to humans. The factor is divided into a factor of 4, which is a size scaling factor for rats, and a factor of 2.5, which takes into account different modes of action
AF2: is an uncertainty factor that takes into account different degrees of sensitivity in the human population. This is by default set to 10 for the general population.

It should be noticed that the dermal DNEL value has been calculated based on data using oral exposure in experimental animals. As no data were available on the dermal and oral absorption rates of the substance, it has not been possible to adjust the oral NOAEL level to a dermal NOAEL. If these data were available the oral NOAEL value should have been adjusted by a factor “f = oral absorption percentage/ dermal absorption percentage”, i.e. a factor typically above 1, and the DNEL would then have been higher than the DNEL that have been calculated above.

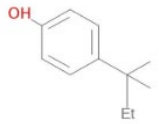
6.2 4-tert-amylphenol (CAS 80-46-6)

6.2.1 General data

The substance is REACH registered in a tonnage band of 100-1000 tonnes per year, i.e. the data requirements for the substance with regard to its hazards are at a medium level. The substance is used as a monomer in the industrial production of phenol-based polymers. The substance has undergone the substance evaluation process under REACH, and it has been concluded that the substance is an SVHC substance due to endocrine disrupting effects in the environment. In the registration dossier, the substance has the following human health hazard classifications: *Skin Corr. 1B H314; Skin Sens. 1 H317, Eye Damage 1 H318.*

TABLE 30 below gives the chemical identity and physiochemical data of the substance.

TABLE 30. 4-tert-amylphenol (CAS 80-46-6)

ID and physicochemical data		Reference
Chemical name	p-(1,1-dimethylpropyl)phenol	REACH-reg. 2024b
Chemical structure		REACH-reg. 2024b
Chemical Formula	$C_{11}H_{16}O$	PubChem
Molecular weight	164.24 g/mol	PubChem
Melting point	94.7 °C	REACH-reg. 2024b
Boiling point	255 °C	REACH-reg. 2024b
Water solubility	193 mg/L at 21 °C	REACH-reg. 2024b
Log Pow	3.6 at 22 °C	REACH-reg. 2024b
Vapour pressure	5 Pa at 20 °C	REACH-reg. 2024b

6.2.2 Toxicological data

As a literature search has not found any additional relevant data regarding human toxicological data for the substance, the assessment is based solely on data from the REACH registration dossier for the substance (REACH reg 2024b).

Acute toxicity

The substance has low acute toxicity and the LD50 is above the classification limit.

Irritation

The substance showed a corrosive effect after 4 hours of exposure to the skin of rabbits, which resulted in the substance being classified in the REACH registration dossier as *Skin Corr. 1B H314; Skin Sens. 1 H317, Eye Damage 1 H318.*

Three minutes of exposure to the skin of rabbits caused a slight degree of irritation on the skin.

Sensitisation
In a Buehler test, guinea pigs were induced with a dermal dose with 50% of the substance in vaseline and then challenged with 10% in vaseline. After challenge, 10 out of 20 guinea pigs reacted with a positive allergic reaction.

In an LLNA test, mice were dosed on the back of the ears with dimethyl sulfoxide solutions containing the substance at concentrations of 25, 50 and 100%. Based on the measurement of the reaction (uptake of radioactivity) in the lymph nodes of the ears (see Figure 4), the following stimulation index values, SI[15] were calculated: 6.91 (25% solution); 9.66 (50% solution) and 8.19 (100% solution). The substance was assessed to be a "moderate" sensitising substance.

Disintegrations per minute (DPM) for each of the test substances (n=5 animals per group), with mean and SD

	DMSO	Hexylcinnamaldehyde	25% PTAP	50% PTAP	100% PTAP
	675.99	4584.96	3344.62	2280.50	1265.70
	551.36	4081.94	2770.56	3232.55	2525.20
	613.92	5164.41	3581.27	6357.37	5007.96
	410.02	5245.38	4408.53	5715.82	7601.05
	227.85	5843.58	3027.46	6360.64	3905.08
Mean	495.83	4984.05	3426.49	4789.38	4061.00
SD	179.35	673.18	629.39	1904.20	2430.30

Figure 3. Values for measured radioactive decay in the lymph nodes of the mouse ears (PTAP: 4-tert-amylphenol) (REACH-reg. 2024b)

Effects of repeated dosing
In a 90-day oral dosing study in rats at dose levels of 0, 50, 200 and 600 mg/kg bw/day, decreased body weight and irritative effects in the stomach of rats were found at the highest dose level, and a systemic NOAEL was established at 200 mg/kg bw/day. Signs of stomach irritation were found even at the lowest dose.

In a 90-day skin exposure study in rats, no systemic effects were observed at the highest dose level of 25 mg/kg bw/day. At 25 mg/kg bw/day and at 10 mg/kg bw/day, with exposure to formulations at test concentrations of 4.17 mg/ml and 1.67 mg/ml respectively (i.e. 0.42% and 0.17% respectively), dose-related signs of skin irritation were observed. Dosing at 2.5 mg/kg bw/day with a formulation at 0.42 mg/mL (i.e. 0.04%) did not cause any skin irritation. This concentration was converted in the REACH dossier to a surface exposure of 20 µg/cm^2.

For reproductive toxicity effects, the REACH dossier uses read-across for data from a two-generation oral study of tert-butylphenol conducted in rats. In this study, a NOAEL of 70 mg/kg bw/day was obtained for the mothers, as the rats had reduced body weight at a dose of 200 mg/kg bw/day. For the offspring, a NOAEL of 70 mg/kg bw/day was also found, as increased mortality of the offspring, reduced body weight and effects on the genitalia of the female rats were found at higher doses. (This study resulted in classification with Repr. 2 in the REACH dossier for tert-butylphenol, but this classification has not been included in the registration dossier for p-tert amylphenol).

[15] SI: the ratio of measured radioactivity measured in lymph nodes from exposed animals compared to the radioactivity measured in control animals

In a study of foetal development with tert-amylphenol, NOAEL and LOAEL of 50 and 200 mg/kg bw/day, respectively, were found for the dams. Apart from a slight, dose-related increase in flexed ribs in the foetuses, no harmful effects were found in the offspring even at the highest dose of 500 mg/kg bw/day.

Mutagenic and carcinogenic effects
The substance showed no mutagenic effects in either bacterial strains or mammalian cells. An *in vivo* micronucleus test also showed no mutagenic/genotoxic effects.

Overall assessment and calculation of DNEL

Irritation
The substance must be considered to be highly irritating as daily dosing on the skin of rats at a concentration as low as 0.17% caused signs of irritation of the skin. The NOAEL for this effect was 0.04% equivalent to 20 µg/cm^2. However, it is uncertain whether the skin effects in the rats were solely due to an irritant effect or whether the animals showed skin reactions as a result of skin sensitisation.

Based on the principles set out in ECHA (2012), the DNEL for irritation can be calculated.

DNEL = NOAEL/ (AF1 x AF2 x AFn)
DNEL = 20 µg/cm^2 /(1 x 10) = 2 µg/cm^2

where
AF1: is set to 1 as humans are not considered more sensitive than laboratory animals for a simple irritative effect
AF2: is an uncertainty factor that takes into account different degrees of sensitivity in the human population. This is by default set to 10 for the general population.

Sensitisation
As data are available from an LLNA test, it is possible to apply the principles stated by Api et al (2020) and further developed by Corea et al. 2023 to calculate an acceptable level of exposure, equivalent to a DNEL for sensitising substances.

From the LLNA data given in the REACH dossier (see Figure 4), an EC3 value (i.e. SI=3) of 8.5% or 11.5% can be calculated using linear extrapolation from the SI values for 25% or 50% 4-tert-amylphenol to the SI value in the DMSO control group.

Based on the lowest EC3 value of 8.5%, the EC3 exposure in an LLNA test can be converted to µg/cm^2 by multiplying the numerical % value by a conversion factor of 250 (Corea et al. 2023). Thus, a concentration of 8.5% corresponds to a skin exposure of 2125 µg/cm^2. This value is used as the NESIL value for the calculation of the DNEL:

This value can then be used to calculate the DNEL.
DNEL = NESIL / SAF1 x SAF2 x SAF3
DNEL = 2125 µg/cm^2 / (1 x 10 x 3)
DNEL = 71 µg/cm^2

where
SAF1: Interspecies factor (set to 1 using LLNA EC3 value from LLNA mouse study (Corea et al. 2023), as data indicate overall compliance between EC3 values and human sensitisation thresholds.
SAF2: Is an uncertainty factor that takes into account different degrees of sensitivity in the human population. This is by default set to 10 for the general population.

SAF3: A value of 3 is used to consider prolonged/repeated exposure.

It should be noted that the calculated DNEL value for sensitisation in this case is significantly higher than the calculated DNEL value for irritation.

Systemic effects
Based on a NOAEL of 25 mg/kg bw/day from a 90-day dermal exposure study in rats, the following dermal DNEL can be calculated according to the principles set out in ECHA (2012):

DNEL = NOAEL / (AF1 x AF2 x AFn)
DNEL = 25 mg/kg bw/day / 10 x 10 x 2 = 0.13 mg/kg bw/day

where
AF1: is an uncertainty factor for extrapolation from animals to humans. The factor of 10 is divided into a factor of 4, which is a size scaling factor for rats, and a factor of 2.5, which takes into account different modes of action.
AF2: is an uncertainty factor that takes into account different degrees of sensitivity in the human population. As default set to 10 for the general population.
AF3: is set at 2 to extrapolate from subchronic exposure to chronic exposure.

It should be noticed that the dermal DNEL value has been calculated based on data using oral exposure in experimental animals. As no data were available on the dermal and oral absorption rates of the substance, it has not been possible to adjust the oral NOAEL level to a dermal NOAEL. If these data were available the oral NOAEL value should have been adjusted by a factor "f = oral absorption percentage/ dermal absorption percentage", i.e. a factor typically above 1, and the DNEL would then have been higher than the DNEL that have been calculated above.

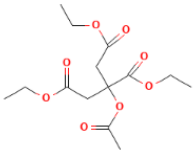
6.3 *o*-Acetyltriethyl citrate (CAS 77-89-4)

6.3.1 General data

The substance is REACH registered in a tonnage band of 100-1000 tons per year. The substance is used in binders and surface treatment agents, as a bulking agent and as a *as* plasticizer. Is also used in finger paints. In the registration dossier, the substance is not classified for any human health hazards.

TABLE 31 below gives the chemical identity and physicochemical data of the substance.

TABLE 31. Physicochemical data for *o*-acetyltriethyl citrate (CAS 77-89-4)

ID and physicochemical data		Reference
Chemical names	Triethyl *o*-acetyl citrate; Triethyl 2-acetoxypropane-1,2,3-tricarboxylate	REACH-reg. 2024c
Chemical structure		PubChem
Chemical Formula	$C_{14}H_{22}O_8$	PubChem
Molecular weight	318.32 g/mol	PubChem
Melting point	-45 °C	REACH-reg. 2024c
Boiling point	294 °C	REACH-reg. 2024c

ID and physicochemical data		Reference
Water solubility	0.07 g/L at 25 °C	REACH-reg. 2024c
Log Pow	1.34 at 25 °C	REACH-reg. 2024c
Vapour pressure	1 Pa at 20 °C	REACH-reg. 2024c

6.3.2 Toxicological data

In addition to the REACH registration dossier of the substance, the literature search found the following expert assessments:

CIR (2002). Final Report on the Safety Assessment of Acetyl Triethyl Citrate, Acetyl Tributyl Citrate, Acetyl Trihexyl Citrate, and Acetyl Trioctyl Citrate. International Journal of Toxicology, 21(Suppl. 2):1–17.

CIR (2019). Safety Assessment of Acetyl Trialkyl Citrates as Used in Cosmetics.

CSTEE (1999). Opinion on the toxicological characteristics and risks of certain citrates and adipates used as a substitute for phthalates as plasticisers in certain soft PVC products. SCIENTIFIC COMMITTEE ON TOXICITY, ECOTOXICITY AND THE ENVIRONMENT. B2/JCD/csteeop/cit28999.D(99)

When reviewing data, the data in the REACH registration is considered to be the best updated and thus the best basis for the assessment.

Kinetics

No data is available for *o*-acetyltriethyl citrate but data for *o*-tributyl citrate indicates complete and rapid absorption of this substance from the gastrointestinal tract and metabolism in the body by hydrolysis of the ester bonds and excretion of metabolites with urine and through faeces.

No data is available on dermal absorption of the substance (CIR 2002, CSTEE 1999).

Acute toxicity

Oral and dermal exposure produce a very low level of acute toxicity and therefore the substance is not classified for acute toxicity (REACH-reg 2024c).

Irritation

No signs of irritation were observed in a skin irritation test in rabbits (REACH-reg 2024c). The substance produced only a mild degree of eye irritation in rabbits (REACH-reg 2024c).

Sensitisation

In a GPMT performed with intradermal induction with a 2.5% test solution followed by dermal induction with the test substance at 100%, and after 14 days, nine out of ten test animals exhibited allergic reactions to dermal challenge with a 50% test solution of the substance (REACH-reg 2024c). Based on this test, CIR (2002) and CSTEE (1999) assess that the substance exhibits a strong sensitising effect.

In a study conducted with human volunteers, no skin irritation or skin sensitisation effects were found among 59 people exposed using patch samples with 0.4 ml of the test substance spread over an area of 400 cm^2. The induction exposure was performed on the upper arm with a duration of 24 hours and was performed three times weekly for three weeks. The challenge exposure was performed after a further two-week period. This study is listed in the REACH registration as the most relevant study for assessing sensitisation, which is why the substance is not classified for sensitisation.

Effects of repeated dosing
The REACH registration indicates that a 28-day oral dosing study in mice had a NOAEL of 400 mg/kg bw/day. It is stated, however, that increased organ weights were found for the kidneys, adrenal glands and testicles, but that this did not lead to histopathological changes in the organs.

It appears from the original reference for this study by Xu et al. (2019) that the animals at 400 mg/kg bw/day exhibited aggressive behaviour, and this was thought to be due to the substance causing hyperactivity in the central nervous system, which has been seen for other citrates. Furthermore, significant dose-related increases in organ weights of the testicles and adrenal glands were found at the two highest dosage levels of 40 and 400 mg/kg bw/day, so that the NOAEL may more reliably be set at 40 mg/kg bw/day or perhaps even at 4 mg/kg bw/day, which was the lowest dose level.

In a separate study by Li et al. (2024), mice were exposed to the substance daily through the feed for 12 weeks at dose levels of 0.1 and 10 µg/kg bw/day. These doses led to increased body weight, increased fat percentage, and increased triglyceride content in the liver. The authors did not derive any NOAEL for this study but pointed out that the substance probably interferes with lipid uptake and lipid metabolism.

Kim et al (2018) conducted a Hersberger study to assess possible androgenic effects of the substance. Over 10 days, young castrated male rats were orally dosed at 40 and 400 mg/kg bw/day. Compared to the control group, dosing with the drug showed weak anti-androgenic effects.

Standard reproduction and foetal development studies are not available for the substance (REACH-reg 2024c).

Mutagenic and carcinogenic effects
The substance has not shown mutagenic effects in *in vitro* studies in bacteria and mammalian cells. An *in vivo* study in mice showed no effect in bone marrow cells at an oral dose of up to 2000 mg/kg bw/day (REACH reg 2024).

Overall assessment and calculation of DNEL

Sensitisation
The substance is sensitising in a GPMT test and based on the response in this test it meets the CLP criteria for Skin Sens. 1B, i.e. a moderate sensitiser. However, it is not considered to be appropriate to include the quantitative data from this study in a quantitative determination of a NESIL value, as the starting point for that would be an EC3 value from an LLNA study.

Similarly, it is not considered appropriate to base the determination on the reported human study (an unpublished study from 1978 with volunteers), in which an induction dose of 0.4 ml over an area of 400 cm^2 (i.e. approx. 1 mg/cm^2) did not cause allergy.

Systemic effects
The available data is very poor as a basis for the determination of a DNEL for systemic effects. A relevant NOAEL is estimated to be in the range of 4-40 mg/kg bw/day based on a 28-day mouse study with oral exposure. Since data are not available for oral or dermal absorption of the substance, the oral NOAEL value was used directly to calculate a dermal DNEL value according to the principles stated by ECHA (2012):

DNEL = NOAEL / (AF1 x AF2 x AFn)
DNEL = 4 - 40 mg/kg bw/day / 17.5 x 10 x 6)

DNEL = 3.8 – 38 µg/kg bw/day

where
AF1: is an uncertainty factor for extrapolation from animals to humans. The factor of 17.5 is divided into a factor of 7, which is a size scaling factor for mice, and a factor of 2.5, which takes differences in modes of action into account.
AF2: is an uncertainty factor that takes into account different degrees of sensitivity in the human population. As default set to 10 for the general population.
AF3: is set to 6 to extrapolate from subacute exposure to chronic exposure

It should be noticed that the dermal DNEL value has been calculated based on data using oral exposure in experimental animals. As no data were available on the dermal and oral absorption rates of the substance, it has not been possible to adjust the oral NOAEL level to a dermal NOAEL. If these data were available the oral NOAEL value should have been adjusted by a factor "f = oral absorption percentage/ dermal absorption percentage", i.e. a factor typically above 1, and the DNEL would then have been higher than the DNEL that have been calculated above.

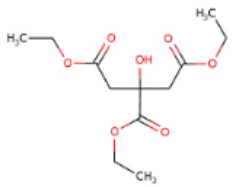
6.4 Triethyl citrate (CAS 77-93-0)

6.4.1 General data

The substance is REACH registered in a tonnage band of 1000 -10000 tonnes per year, i.e. there are extensive data requirements for the substance with regard to its hazards. The substance is used in products for surface treatment/sealing, in detergents, as well as in cosmetics and as a food additive. The registration dossier does not provide any classification for the substance.

TABLE 32 gives the chemical identity and physicochemical data of the substance.

TABLE 32. Physicochemical data for triethyl citrate (CAS 77-93-0)

ID and physicochemical data		Reference
Chemical name	Triethyl citrate	REACH-reg. 2024d
Chemical structure		REACH-reg. D
Chemical Formula	$C_{12}H_{20}O_7$	REACH-reg. 2024d
Molecular weight	276,28 g/mol	PubChem
Melting point	-40 °C	REACH-reg. 2024d
Boiling point	286.8 °C	REACH-reg. 2024d
Water solubility	58.1 g/L at 20 °C	REACH-reg. 2024d
Log Pow	1.17 at 40 °C	REACH-reg. 2024d
Vapour pressure	0.3 Pa at 25 °C	REACH-reg. 2024d

6.4.2 Toxicological data

In addition to the REACH registration dossier of the substance, the following relevant references have been found in the literature search:

JECFA (1979). Safety evaluation of certain food additives. Additives and contaminants. WHO additives series: 14. 485. Triethyl Citrate (WHO Food Additives Series 14) (inchem.org)

JECFA (2000). Safety evaluation of certain food additives. Additives and contaminants. WHO additives series: 44. 974. Esters containing additional oxygenated functional groups (WHO Food Additives Series 44) (inchem.org)

CIR (2014). Safety Assessment of Citric Acid, Inorganic Citrate Salts, and Alkyl Citrate Esters as Used in Cosmetics. International Journal of Toxicology 2014, Vol. 33(Supplement 2) 16S-46S.

For all references, the data are predominantly older, and the way of reporting of data is very poor for all sources, which makes the assessment of the substance very uncertain.

Acute toxicity
There are a lot of older data concerning the acute toxicity of the substance. All the LD50 values listed are significantly above the classification limit for acute toxicity.

Irritation
The data on irritation are generally old and of poor quality. However, both the REACH registration and CIR (2014) indicate a very low degree of irritation of the substance based partly on animal study data and human data.

Sensitisation
In a GPMT test performed with intradermal induction with a 2.5% test solution followed by dermal induction with 100% of the substance and then dermal challenge with a 50% test solution of the substance, nine out of nine guinea pigs reacted with positive allergic response (CIR (2014) and REACH-reg 2024d).

CIR (2014) refers to eight unpublished human studies in which induction exposure and subsequent challenge exposure to the substance did not cause allergic reactions. However, the studies are very poorly reported: among other things, the test concentrations are stated as unknown in seven of the studies.

Effects of repeated dosing
JECFA (1979 + 2000) reports a NOAEL of 4000 mg/kg bw/day from a 2-month oral study in rats, while a LOAEL of 285 mg/kg bw/day is reported from a 2-month feeding study in cats, with weakness, uncoordinated movements and lethargy occurring at this dose.

The REACH registration dossier reports a NOAEL of 600 mg/kg bw/day from an older 2-year feeding study in rats. It should be noted that it is reported that there were only four rats in each dose group in this study.

Based on read-across from acetyl tributyl citrate, the REACH registration dossier indicates a NOAEL of 1000 mg/kg bw/day for reproductive toxicity from a 90-day oral dosing reproduction study in rats.

Mutagenic and carcinogenic effects
Mutagenesis tests performed with bacteria and yeast cells showed no mutagenic activity of the substance.

Overall assessment and calculation of DNEL

Sensitisation

The substance is sensitising in a GPMT test and based on the response in this test it meets the CLP criteria for Skin Sens. 1B, i.e. a moderate sensitiser. However, it is not considered to be appropriate to include the quantitative data from this study in a quantitative determination of a NESIL value, as the starting point for that would be an EC3 value from an LLNA study.

Similarly, the reported human studies are not considered suitable for quantitative assessment for the determination of NESIL.

Systemic effects
Data for the substance are considered unsuitable for the calculation of the DNEL.

In their assessment of the substance as a food additive, JECFA has determined an ADI value of 0-20 mg/kg bw/day and assesses the substance as safe for use as a food additive, as the substance occurs naturally in the body as part of the metabolic tricarboxylic acid cycle.

No systemic DNEL is calculated for this substance, partly due to lack of suitable data and partly because the substance is considered by JECFA to have low oral toxicity.

6.5 Summary

When reviewing the toxicological data for the selected substances for risk assessment, the following DNELs given in TABLE 33 have been derived.

TABLE 33. DNELs for dermal exposure for four selected substances

	DNEL (irritation)	DNEL (sensitisation)	DNEL systemic
drometrizole	Irritation not a critical effect	Sensitising, but data not suitable for DNEL calculation*	470 µg/kg bw/day
4-tert-amylphenol	2 µg/cm^2	71 µg/cm^2	130 µg /kg bw/day
***o*-acetyltriethyl citrate**	Irritation not a critical effect	Sensitising, but data not suitable for DNEL calculation*	3.8 – 38 µg/kg bw/day
triethyl citrate	Irritation not a critical effect	Sensitising, but data not suitable for DNEL calculation*	Not applicable due to low toxicity

*A DST value of 73 µg/cm^2 is used to assess exposure to these substances (see below).

As shown in the table, for the substances triethyl citrate, *o*-acetyl triethyl citrate and drometrizole it was not possible to calculate a DNEL for sensitisation using the QRA2 method, where the starting point for the calculation is an EC3 value from an LLNA test.

As mentioned in the substance assessments above, the three substances can be classified as Skin Sens. 1B, i.e. skin sensitising substances with moderate potency, based on the GPMT tests performed according to the CLP criteria.

In order to distinguish between high, medium and low potency skin sensitisers, Chilton et al. (2022) performed statistical analyses on the distribution of EC3 values from LLNA tests for a number of sensitising substances characterised as non-reactive (79 substances), reactive (331 substances) and highly reactive (146 substances). Grouping of the reactivity of the substances was performed using a Derek Nexus QSAR programme. Chilton et al (2022) then used the lowest 5% percentile of the EC3 values in the three groups as the Dermal Sensitisation Threshold (DST).

For the non-reactive, reactive and highly reactive sensitisers, the DST values were set at 710 µg/cm2, 73 µg/cm^2 and 1 µg/cm^2 respectively.

To put the exposure to triethyl citrate, *o*-acetyltriethyl citrate and drometrizole into perspective, the substances as moderate sensitisers may be considered in the intermediate group of reactive substances: it is therefore considered relevant to assess exposure to these substances with a proposed *DST value of 73 µg/cm^2*. This value will be used in the following as a provisional value in the risk assessment of the three substances.

7. Risk assessment

7.1 Methodology

The first step in the risk assessment is to calculate the exposure to the substances based on the analytical results obtained and the principles outlined in section 3.5. This means that the exposure per cm^2 skin is determined from the analytical results in order to use this measure to assess the risk of local skin effects: skin irritation and skin sensitisation.

Next, the total surface exposure is calculated in µg/kg bw/day as this exposure measure is used in the risk assessment to assess effects after possible absorption into the body.

The risk assessment itself is then performed by comparing the exposure values with the tolerable exposure levels for the substances (i.e. the DNELs calculated in the hazard assessment section in Chapter 5).

This is done by calculating the risk characterisation ratio, RCR, according to ECHA (2016):

RCR = exposure value / DNEL value

In cases where the exposure exceeds the DNEL, the RCR value will be greater than 1, indicating that there is a potential risk associated with the exposure.

In cases where the exposure is below the DNEL, the RCR will be less than 1, indicating that the exposure poses no risk.

In borderline cases, where the RCR is just above or just below 1, it will be necessary to further analyse the data in terms of uncertainties in the calculations and assumptions made in the exposure assessment and in setting the DNEL.

7.2 Exposure assessment

Local exposure on skin in contact with the frame
TABLE 27 above shows the analysis results for the amount of substance released per cm^2 of spectacle frame after 72 hours of migration. The values can be used as a worst-case estimate of how much skin is exposed per cm^2 of skin per day by dividing the 72-hour value by 18 hours/72 hours, assuming that the spectacles are worn up to 18 hours per day. The calculation assumes that the spectacles release the same amount of substance per cm^2 over time as measured in the migration analyses.

In TABLE 34 below, the results from TABLE 27 are therefore adjusted by a factor of 0.25, corresponding to 18 hours/72 hours.

TABLE 34. Daily skin exposure per cm^2

Spectacle frames	Drometrizole	4-tert-amylphenol	*o*-acetyltriethyl citrate	Triethyl citrate
Spectacles 4	5.8 µg/cm^2	-	3.3 µg/cm^2	0.48 µg/cm^2
Spectacles 11	6.0 µg/cm^2	-	965 µg /cm^2	11 µg/cm^2
Spectacles 13	6.8 µg/cm^2	0.0025 - 0.01 µg/cm^2	4300 µg/cm^2	89 µg/cm^2

Spectacle frames	Drometrizole	4-tert-amylphenol	*o*-acetyltriethyl citrate	Triethyl citrate
Spectacles 16	-	-	11 µg/cm^2	0.63 µg/cm^2
Spectacles 17	8.0 µg/cm^2	1.3 µg/cm^2	1.2 µg/cm^2	0.10 µg/cm^2
Spectacles 18	8.3 µg/cm^2	0.02 µg/cm^2	1.2 µg/cm^2	0.13 µg/cm^2

Total exposure from contact with spectacle frames
The total exposure from a spectacle frame can be calculated from the daily substance release per cm^2 of frame multiplied by the area of the frame in contact with the user's skin.

It is difficult to give an exact figure for the contact area of each frame in relation to a user, as this depends on how much of the temples that are in close contact to the user's skin, behind the ears and on the bridge of the nose.

However, based on the design of the frames and the width of the temples, it is estimated that worst-case estimates can be made, that ca. 10 cm of the temples will be in close contact with the skin at each site of the head, and that the contact on the bridge of the nose is approximately 2 x 1 cm^2.

For spectacles nos. 4, 11 and 13, the width of the temples was measured, and from this the total area of skin contact can be calculated as shown in TABLE 35. The temples are not equally wide over the 10 cm assumed to be in contact with the skin, so the average width of the narrowest and widest part of the temple was used.

TABLE 35. Contact surface of the spectacles

Spectacle frames	Contact width temple	Contact length temple	Contact surface temple	Contact surface nose bridge	Total contact surface
Spectacles 4*	0.43 cm	2 x 8 cm	6.9 cm2	2 cm^2	8.9 cm^2
Spectacles 11	0.51 cm	2 x 10 cm	10.2 cm2	2 cm^2	12.2 cm^2
Spectacles 13	0.35 cm	2 x 10 cm	7.0 cm2	2 cm^2	9.0 cm^2

*children's frames

For the other frame materials tested, an average of these worst-case considerations is taken, so that the contact area for the other spectacles is estimated to be 10.6 cm^2 in the exposure calculations.

The total exposure (substance released on the skin of the user) in µg/kg bw/day per day can then be calculated from the following expression

Total exposure (µg/kg bw/day) = total contact area (cm^2) x daily release per cm^2 (µg/cm^2/day) / 60 kg

ECHA (2016a) uses a body weight of 60 kg for women in the context of risk assessments. For spectacle frame 4, which is a children's frame, the project group estimated that the target group could be 10–12-year-old girls based on the appearance and dimensions of the frame. Based on the growth curve for Danish girls, a body weight of 35 kg is used for this target group.

In TABLE 36 below, the values from TABLE 34 (daily release per cm^2) and TABLE 35 (total skin contact area) are used to calculate the daily amount of substance deposited on the user's skin at the contact points per kg body weight.

TABLE 36. Estimated total skin exposure (µg/kg bw/day)

Spectacle frames	Total contact surface	Drometrizole µg/kg bw/day	4-tert-amylphenol µg/kg bw/day	*o*-acetyltriethyl citrate µg/kg bw/day	Triethyl citrate µg/kg bw/day
Spectacles 4	8.9 cm^2	1.5	-	0.84	0.12
Spectacles 11	12.2 cm^2	1.2	-	196	0.40
Spectacles 13	9.0 cm^2	1.0	0.0015	645	13
Spectacles 16	10.6 cm^2	-	-	1.9	0.11
Spectacles 17	10.6 cm^2	1.4	0.23	0.21	0.018
Spectacles 18	10.6 cm^2	1.5	0.0035	0.21	0.023

7.3 Risk assessment

In the following risk assessment, RCR values are calculated using the formula

RCR = Exposure value / DNEL value

The calculation of RCR values for systemic effects is based on the worst-case assumption that the absorption of dermal exposure is equal to the oral absorption used in the animal studies to identify the critical NOAEL and to calculate the DNEL. This means that the calculations do not adjust for potentially lower absorption by dermal route compared to oral route.

7.3.1 Risk assessment of the individual frames

Spectacle frame 4
Below in TABLE 37, RCR values are calculated for the quantitative findings of triethyl citrate, *o*-acetyltriethyl citrate and drometrizole.

TABLE 37. Spectacles 4, risk assessment

	Local effects		
Substance	**Exposure µg/cm^2**	**DNEL µg/cm^2**	**RCR**
4-*tert*-amylphenol	-	2 irr 71 sens	-
Triethyl citrate	0.48	73*	0.006
***o*-acetyltriethyl citrate**	3.3	73*	0.05
Drometrizole	5.8	73*	0.08
	Systemic effects		

Substance	Exposure µg/ kg bw/ day	DNEL µg/ kg bw/ day	RCR
4-*tert*-amylphenol	-	130	-
Triethyl citrate	0.12	-	-
***o*-acetyltriethyl citrate**	0.84	3.8-38	0.02-0.2
Drometrizole	1.5	470	0.003

*General threshold value for moderate sensitising substances (Chilton et al. 2022)

The table indicates very low RCR values, and the migration of the three substances is not considered to pose any risk of harmful effects.

The migration fluid was a faint pink liquid from unknown colourants, which is why the risk from dyes cannot be further assessed.

Spectacle frame 11
Below in TABLE 38, RCR values are calculated for the quantitative findings of triethyl citrate, *o*-acetyltriethyl citrate and drometrizole.

TABLE 38. Spectacles 11, risk assessment

Local effects			
Substance	**Exposure** **µg/cm²**	**DNEL** **µg/cm²**	**RCR**
4-*tert*-amylphenol	- -	2 irr 71 sens	- -
Triethyl citrate	11	73*	0.15
***o*-acetyltriethyl citrate**	965	73*	**13**
Drometrizole	6.0	73*	0.08
Systemic effects			
Substance	**Exposure** **µg/ kg bw/ day**	**DNEL** **µg/ kg bw/ day**	**RCR**
4-*tert*-amylphenol	-	130	-
Triethyl citrate	0.40	-	-
***o*-acetyltriethyl citrate**	196	3.8-38	**5.2-52**
Drometrizole	1.2	470	0.003

*General threshold value for moderate sensitising substances (Chilton et al. 2022)

For frame 11, the exposure to *o*-acetyltriethyl citrate is much higher than to the other substances and the RCR values for this substance for sensitisation and long-term systemic effects indicate a risk from migration with this substance.

The exposure levels and low RCR values for triethyl citrate and drometrizole do not give rise to health concerns for migration of these substances.

The migration fluid, which was a dark blue liquid, contained Solvent Orange 60 and Solvent Red 179 in the screening analysis. Skin allergy has been observed for both of these dyes

when used in spectacle frames, so there may be a potential sensitisation risk due to migration of these two substances.

Spectacle frame 13
Below in TABLE 39, RCR values are calculated for the quantitative findings of 4-tert-amylphenol, triethyl citrate, *o*-acetyltriethyl citrate and drometrizole.

TABLE 39. Spectacles 13, risk assessment

Local effects			
Substance	**Exposure µg/cm²**	**DNEL µg/cm²**	**RCR**
4-*tert*-amylphenol		2 irr	0.005
	0.01	71 sens	0.0001
Triethyl citrate	89	73*	**1.2**
***o*-acetyltriethyl citrate**	4300	73*	**58**
Drometrizole	6.8	73*	0.09
Systemic effects			
Substance	**Exposure µg/ kg bw/ day**	**DNEL µg/ kg bw/ day**	**RCR**
4-*tert*-amylphenol	0.0015	130	0.00001
Triethyl citrate	13	-	-
***o*-acetyltriethyl citrate**	645	3.8-38	**17-170**
Drometrizole	1.0	470	0.002

*General threshold value for moderate sensitising substances (Chilton et al. 2022)

For spectacle frame 13, the exposure to *o*-acetyltriethyl citrate far exceeds the other substances and the RCR values for this substance in terms of sensitising effect and long-term systemic effects indicate a risk from migration with this substance. For triethyl citrate, an RCR value of 1.2 is observed, i.e. a slight exceedance of the DST value, while no risk of long-term effects is assessed for this substance.

The exposure levels and the very low RCR values for 4-tert-amylphenol and drometrizole do not give rise to health concerns due to migration of these substances.

The migration fluid was a colourless liquid and therefore the risk related to dyes is not relevant.

Spectacle frame 16
Below in TABLE 40, RCR values are calculated for the quantitative findings of triethyl citrate and *o*-acetyltriethyl citrate.

TABLE 40. Spectacles 16, risk assessment

Local effects			
Substance	**Exposure µg/cm²**	**DNEL µg/cm²**	**RCR**
4-*tert*-amylphenol		2 irr	-
	-	71 sens	-

Local effects			
Substance	**Exposure µg/cm²**	**DNEL µg/cm²**	**RCR**
Triethyl citrate	0.63	73*	0.009
***o*-acetyltriethyl citrate**	11	73*	0.15
Drometrizole	-	73*	-
Systemic effects			
Substance	**Exposure µg/ kg bw/ day**	**DNEL µg/ kg bw/ day**	**RCR**
4-*tert*-amylphenol	-	130	-
Triethyl citrate	0.11	-	-
***o*-acetyltriethyl citrate**	1.9	3.8-38	0.05-0.50
Drometrizole	-	470	-

*General threshold value for moderate sensitising substances (Chilton et al. 2022)

For frame 16, the highest exposure is observed for *o*-acetyl triethyl citrate compared to tritethyl citrate. However, the RCR values for both substances are less than 1 and no risk is considered to be associated with the migration of these substances.

The migration fluid was an intense brown/orange liquid, which in the screening analysis contained Solvent Orange 60. Skin allergy has been observed to this dye when used in spectacle frames, so there may be a potential sensitisation risk due to migration of the substance.

Spectacle frames 17
Below in TABLE 41, RCR values are calculated for the quantitative findings of 4-tert-amylphenol; triethyl citrate, *o*-acetyltriethyl citrate and drometrizole.

TABLE 41. Spectacles 17, risk assessment

Local effects			
Substance	**Exposure µg/cm²**	**DNEL µg/cm²**	**RCR**
4-*tert*-amylphenol	1.3 1.3	2 irr 71 sens	0.65 0.018
Triethyl citrate	0.10	73*	0.001
***o*-acetyltriethyl citrate**	1.2	73*	0.02
Drometrizole	8.0	73*	0.11
Systemic effects			
Substance	**Exposure µg/ kg bw/ day**	**DNEL µg/ kg bw/ day**	**RCR**
4-*tert*-amylphenol	0.23	130	0.002
Triethyl citrate	0.018	-	-
***o*-acetyltriethyl citrate**	0.21	3.8-38	0.06 – 0.006
Drometrizole	1.4	470	0.003

*General threshold value for moderate sensitising substances (Chilton et al. 2022)

For frame 17, the highest RCR value of 0.65 is obtained for exposure to 4-tet-amylphenol in relation to irritation. All the other RCR values are well below 1 and, overall, there is no risk associated with the migration of the four substances found.

The migration fluid was a pale pink liquid containing CI Solvent Yellow 1 in the screening analysis. The substance is classified as a carcinogen, but due to the lack of quantitative data it is not possible to assess a potential cancer risk.

Spectacle frames 18
Below in TABLE 42, RCR values are calculated for the quantitative findings of 4-tert-amylphenol; triethyl citrate, *o*-acetyltriethyl citrate and drometrizole.

TABLE 42. Spectacles 18, risk assessment

Local effects			
Substance	**Exposure µg/cm²**	**DNEL µg/cm²**	**RCR**
4-*tert*-amylphenol		2 irr	0.01
	0.02	71 sens	0.0003
Triethyl citrate	0.13	73*	0.002
***o*-acetyltriethyl citrate**	1.2	73*	0.02
Drometrizole	8.3	73*	0.11
Systemic effects			
Substance	**Exposure µg/ kg bw/ day**	**DNEL µg/ kg bw/ day**	**RCR**
4-*tert*-amylphenol	0.0035	130	0.00003
Triethyl citrate	0.023	-	-
***o*-acetyltriethyl citrate**	0.21	3.8-38	0.006- 0.06
Drometrizole	1.5	470	0.003

*General threshold value for moderate sensitising substances (Chilton et al. 2022)

For spectacle frame 18, the low exposure levels for the four substances and the low RCR values obtained do not raise concern for either local or systemic effects.

The migration fluid, which was a red liquid, showed content of Disperse Orange 3 and Disperse Red 1 in the screening analysis. Skin allergy has been observed for both of these dyes when used in spectacle frames, so there may be a potential sensitisation risk due to migration of these two substances.

7.4 Uncertainties in the assessments

The above risk assessments are subject to varying degrees of uncertainty and discussion of these is considered particularly relevant in cases where the RCR values are above or close to 1. In the many cases where the RCR values are well below 1, the uncertainties are considered less critical to the outcome of the risk assessment. The uncertainties in the risk assessments can be partly attributed to uncertainties in the exposure assessment and partly to uncertainties in the hazard assessment.

Uncertainties, exposure

The exposure assessment is based on a single migration test, i.e. a test design that simulates migration within the first 72 hours of use of the frame. Therefore, it is not known whether the same level of migration will occur during longer periods of use. It is conceivable that migration will decrease after the substances in the outermost layer of the frame have been released. In other words, daily exposure will most likely decrease over a longer period of time. It is therefore considered that the exposure assessment is overestimated in terms of long-term exposure. A more accurate measure of long-term exposure could therefore be obtained by performing repeated migration analyses over a longer period. This will be particularly relevant for frames 11 and 13, where a risk associated with long-term exposure to *o*-acetyltriethyl citrate has been identified.

There are also uncertainties in the calculation of the total skin contact area of the frames. However, as the uncertainties relate to surface measurements of the specific frames, the uncertainties are considered to be relatively small and not critical to the risk assessment. As a worst-case scenario, it is assumed that a frame length of 10 cm is in contact with the skin at each side of the head.

The uncertainties related to the body weight of the user and the calculation of the dose per kg body weight are also considered to be relatively limited and not significant.

The exposure estimates expressed in $\mu g/cm^2$ for the assessment of local effects are considered to be valid for shorter exposure periods, and the assessment for local effects (irritation and sensitisation) is considered to be less uncertain.

Uncertainties, risk assessment

For the spectacle frames for which a risk has been identified, *o*-acetyl triethyl citrate and triethyl citrate are the critical substances and it is therefore relevant to assess the uncertainties associated the hazard assessments of these substances.

The data for assessing the sensitising effect of the substances are equivocal, as older GPMT tests indicate a sensitising effect, while human data indicate the opposite. Testing according to the newer guidelines for skin sensitisation testing could clarify whether the substances can be concluded as skin sensitising and at which potency.

Further, recent data for *o*-acetyltriethyl citrate suggest that 28 days of oral administration at 4 and 40 mg/kg bw/day causes significant increases in kidney, adrenal and testis weights in mice and where the consequences of this is unclear. In addition, the substance produced anti-androgenic effects in a Hersberger test. Thus the basis for calculating a DNEL for long-term exposure is considered preliminary and uncertain.

An additional uncertainty is the use of an oral DNEL for assessing dermal exposure, as there are no data to adjust for a potentially lower bioavailability of the substance through skin contact compared to the oral exposure. Therefore, the same uptake from skin is assumed as for oral exposure, which is likely to overestimate the real skin exposure.

Risk assessment, uncertainties

With regard to the risk of skin sensitisation associated with exposure to *o*-acetyltriethyl citrate, this was derived from the exposure assessment in relation to a general DST value for moderately potent skin sensitisers, resulting in high RCR values (RCR = 13 for frame 11 and RCR = 54 for frame 13). On this basis, and as the threshold for sensitising effects is very difficult to determine, migration of *o*-acetyltriethyl citrate from these two frames is considered to pose a risk of sensitisation.

Similarly, high RCRs were found for long-term exposure to *o*-acetyltriethyl citrate from frames 11 and 13. However, the uncertainties in relation to exposure estimation over time and the DNEL derivation for this substance are considered to be so large for a clear risk assessment conclusion.

7.5 Summary and discussion

TABLE 43 below gives an overview of the risk assessment of the six tested frames. It should be noted that the risk assessment is based solely on the migration of the four focus substances, *4-tert-amylphenol, o-acetyltriethyl citrate, triethyl citrate and drometrizole*, and for the colourants found in the TLC extracts in the screening analyses. It should also be noted that the colourants listed in the table have only been identified in the TLC screenings carried out and therefore no attempt has been made to identify them in the migration fluid. The fact that the migration fluid is coloured may be due to one of the dyes identified in the TLC screening, but it may also be due to other dyes as the migration fluid was *not* TLC screened.

TABLE 43. Overview of the risk assessment of the six analysed spectacle frames

	Risk assessment for migration of 4-*tert*-amylphenol *o*-acetyltriethyl citrate triethyl citrate Drometrizole			**Risk assessment for qualitative findings in TLC extract of Solvent Orange 60; Solvent Red 179; CI Solvent Yellow 1; Disperse Orange 3; Disperse Red 1**
	Local effects	**Systemic effects**	**Critical substance**	**Dye in TLC extract Potential risk**
Spectacles 4	No risk	No risk	-	Faint pink migration fluid. No findings of the above mentioned dyes.
Spectacles 11	Potential risk, sensitisation	Potential risk*	Acetyltriethyl citrate	Dark blue migration fluid. Solvent Oange 60 and Solvent Red 179. Skin allergy has been observed for both when used in spectacle frames. Possible sensitisation risk.
Spectacles 13	Potential risk, sensitisation	Potential risk*	Acetyltriethyl citrate (triethyl citrate)	Colourless migration fluid. No detection of the above mentioned dyes.
Spectacles 16	No risk	No risk	-	Strong brown/orange migration fluid. Solvent Orange 60 for which skin allergy has been observed when used in spectacle frames. Possible sensitisation risk.
Spectacles 17	No risk	No risk	-	Faint pink migration fluid. CI Solvent Yellow 1. The substance has an EU harmonised classification with Carc 1B H350. Unknown risk.
Spectacles 18	No risk	No risk	-	Red migration fluid. Disperse Orange 3 and Disperse Red 1. Skin allergy has been observed for both substances when used in spectacle frames. Possible sensitisation risk.

*Indicates that the calculated risk is subject to high uncertainty

Both *o*-acetyltriethyl citrate and triethyl citrate (possibly a degradation product of the plasticiser *o*-acetyltriethyl citrate) migrate in such large quantities from frame no. 11 (*o*-acetyltriethyl citrate only) and frame no. 13 (both substances) that a possible risk of skin sensitisation to these substances is assessed from both frames. With regard to the risk of systemic effects from these frames, the evidence is considered to be very weak due to large uncertainties in the assessment.

The migration fluid was visibly coloured after frames no. 4, 11, 16, 17 and 18 were left in the migration fluid (ethanol and water) at 37°C for three days. This shows that some of the dyes can migrate out of the temples. However, this project did not investigate which dyes migrate into the migration fluid, but for frames no. 11, 16, 17 and 18, different allergenic dyes were observed in the TLC extract (where different organic solvents were used to dissolve the different materials) during the screening analyses. Therefore, there is a possible allergy risk from allergenic dyes, but this was not investigated further as other allergenic substances were prioritised in the project.

It should be noted that there were several other substances identified in the screening analyses that were not investigated further in this project. For example, phthalates were identified among the most significant peaks in almost all frames (except frame 15). Several different phthalates were identified, but DEP was identified in most frames and at levels of 10% or more. However, the identified phthalates have in common that they do not have a classification of concern and were therefore not selected for subsequent migration analysis and risk assessment.

In addition, the antioxidant BHT, a suspected endocrine disruptor, was identified in five of the 19 images, but the substance was identified at very low levels and was therefore not prioritised for migration analysis or risk assessment.

Finally, it should be noted that not all substances could be identified when reviewing the chromatograms from the GC-MS screening. There were some larger peaks which appeared to be various antioxidants or UV stabilisers or other substances. Several images of the same material contain groups of additives that could not be identified, but which recurred in the samples.

Therefore, this project did not look at all the relevant substances in eyewear materials but selected and prioritised the allergenic substances that appeared to be present in the highest concentrations according to the screening.

References

Ahrensbøll-Friis, U., Simonsen, A. B., Dahlin, J., Isaksson, M., Zachariae, C., & Johansen, J. D. (2022). Allergic contact dermatitis from dyes used in the temple of spectacles. Contact Dermatitis, 86(1), 25-28.

Andersen, K. E., Vestergaard, M. E., & Christensen, L. P. (2014). Triethylene glycol bis (2-ethylhexanoate)–a new contact allergen identified in a spectacle frame. Contact Dermatitis, 70(2), 112-116.

Api et al. (2008). Implementation of the dermal sensitization Quantitative Risk Assessment (QRA) for fragrance ingredients. Regulatory Toxicology and Pharmacology 52 (2008) 53–61.

Api et al. (2020). Updating exposure assessment for skin sensitization quantitative risk assessment for fragrance materials. Regulatory Toxicology and Pharmacology 118 (2020) 104805

Batchelor, R. J., & Wilkinson, S. M. (2006). Contact allergy to disperse dyes in plastic spectacle frames. Contact dermatitis, 54(1), 66-67.

Chilton et al. (2022). Updating the Dermal Sensitisation Thresholds using an expanded dataset and an *in silico* expert system. Regulatory Toxicology and Pharmacology 133 (2022) 105200. https://doi.org/10.1016/j.yrtph.2022.105200CIR (2002). Final Report on the Safety Assessment of Acetyl Triethyl Citrate, Acetyl Tributyl Citrate, Acetyl Trihexyl Citrate, and Acetyl Trioctyl Citrate. International Journal of Toxicology, 21(Suppl. 2):1–17.

CIR (2008). Amended Final Report of the Safety Assessment of Drometrizole as used in Cosmetics. International Journal of Toxicology, 27(Suppl. 1):63–75. Amended Final Report of the Safety Assessment of Drometrizole as used in Cosmetics1 (sagepub.com)

CIR (2019). Safety Assessment of Acetyl Trialkyl Citrates as Used in Cosmetics.

CIR (2014). Safety Assessment of Citric Acid, Inorganic Citrate Salts, and Alkyl citrate Esters as Used in Cosmetics. International Journal of Toxicology 2014, Vol. 33(Supplement 2) 16S-46S. 974. Esters containing additional oxygenated functional groups (WHO Food Additives Series 44) (inchem.org)

Connolly, M. C., Kirby, B., Bhushan, M., O'Driscoll, J. B., & Beck, M. H. (2001). Occupational allergic contact dermatitis from methylchloroisothiazolinone and methylisothiazolinone (MCI/MI) in a silicone-emulsion lock lubricant. Contact dermatitis, 44(4), 246-263.

Corea et al. (2023). Assessing the risk of induction of skin sensitization to plant protection products: A quantitative approach. Regulatory Toxicology and Pharmacology 141 (2023) 105408.

Crépy, M. N., Bensefa-Colas, L., Krief, P., Langlois, E., Guillemot, M., & Choudat, D. (2011). Facial leucoderma following eczema: a new case induced by spectacle frames. Contact dermatitis, 65(4), 243-245.

CSTEE (1999). Opinion on the toxicological characteristics and risks of certain citrates and adipates used as a substitute for phthalates as plasticisers in certain soft PVC products. SCIENTIFIC COMMITTEE ON TOXICITY, ECOTOXICITY AND THE ENVIRONMENT. B2/JCD/csteeop/cit28999.D(99)

ECHA (2012). Guidance on information requirements and chemical safety assessment Chapter R.8: Characterisation of dose [concentration]-response for human health. COVER PAGE (europa.eu)

ECHA (2016a). Guidance on Information Requirements and Chemical Safety Assessment Chapter R.15: Consumer exposure assessment. Version 3.0.

ECHA (2016b). Guidance on Information Requirements and Chemical Safety Assessment Part E: Risk Characterisation. Version 3.0.

ECHA, (2019). Annex XV Restriction Report. Proposal for a restriction. Substance name(s): skin sensitizing substances. Version number: 1.2. Date: 14 June 2019. Available at: https://echa.europa.eu/documents/10162/22a89de7-0d13-8edc-f0f9-05f37dcdaec2

ECHA (2021). Assessment of regulatory needs Authority: ECHA Date: 19/11/2021 Group Name: Substances containing 4-tert-butylphenol. Link: ecc8d88f-48eb-3d1c-b3b1-e12edd448f9a (europa.eu)

El-Houri, R. B., Christensen, L. P., Persson, C., Bruze, M., & Andersen, K. E. (2016). Methylisothiazolinone in a designer spectacle frame–a surprising finding. Contact Dermatitis, 75(5), 310-312.

EN ISO 10993-1:2020. Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process

EN ISO 10993-17:2023. Biological evaluation of medical devices – Part 17: Toxicological risk assessment of medical device constituents.

EN ISO 10993-18:2020. Biological evaluation of medical devices – Part 18: Chemical characterisation of medical device materials within a risk management process

Fleischer, R. L., Meyer, N. R., Hadley, S. A., MacDonald, J., & Cavallo, A. (2001). Personal radon dosimetry from eyeglass lenses. Radiation protection dosimetry, 97(3), 251-258.

Hadley, S. A., Meyer, N. R., Fleischer, R. L., & Cavallo, A. (2000). Eyeglass lenses for personal radon dosimetry. *Health physics*, *79*(3), 242-250.

Health Canada (2021). Draft Screening Assessment Benzotriazoles and Benzothiazoles Group. Microsoft Word - 20210302-DSAR Benzotriazoles and benzothiazole-EN-published.docx (canada.ca)

Herkert, N. J., Kassotis, C. D., Zhang, S., Han, Y., Pulikkal, V. F., Sun, M., ... & Stapleton, H. M. (2022). Characterization of per-and polyfluorinated alkyl substances present in commercial anti-fog products and their in vitro adipogenic activity. Environmental Science & Technology, 56(2), 1162-1173.

Ikarashi et al. (1994). Contact sensitivity of and cross-sensitivity between 2-(2 ’ -hydroxy-5 ’ -methylphenyl)benzotriazole (Tinuvin@ P) and 242 ’ -hydroxy-3 ’ -tert-butyl-5 ’ - methylphenyl)-Schlorobenzotriazole (Tinuvin@326) evaluated by lymph node cell proliferation and ear swelling response in mice. Toxicology Letters 71 (1994) 151-159

JECFA (1979). Safety evaluation of certain food additives. Additives and contaminants. WHO additives series: 14. 485. Triethyl Citrate (WHO Food Additives Series 14) (inchem.org)

JECFA (2000). Safety evaluation of certain food additives. Additives and contaminants. WHO additives series: 44. 974. Esters containing additional oxygenated functional groups (WHO Food Additives Series 44) (inchem.org)

Kim, I. S., Yoo, K. H., Kim, M. N., Hong, H. K., Choi, Y. S., Jo, Y. C., ... & Lee, J. S. (2013). The fine scratches of the spectacle frames and the allergic contact dermatitis. Annals of dermatology, 25(2), 152-155.

Kim et al. (2018). Hershberger Assays for Di-2-ethylhexyl Phthalate and Its Substitute Candidates. Dev. Reprod. Vol. 22, No. 1, 19-27. DOI: https://doi.org/10.12717/DR.2018.22.1.019

Lee et al. (2019). Risk Assessment of Drometrizole, a Cosmetic Ingredient used as an Ultraviolet Light Absorber. Toxicol. Res. Vol. 35, No. 2, pp. 119-129 (2019). https://doi.org/10.5487/TR.2019.35.2.119

Li et al. (2024). Plasticizer acetyl triethyl citrate (ATEC) induces lipogenesis and obesity. Toxicology and Applied Pharmacology 482 (2024) 116788

Magnano, G. C., Marussi, G., Adami, G., Crosera, M., & Filon, F. L. (2022). Assessment of dermal absorption of beryllium and copper contained in temple tips of eyeglasses. Toxicology Letters, 361, 64-71.

Nakada, T., & Maibach, H. I. (1998). Eyeglass allergic contact dermatitis. Contact dermatitis, 39(1), 1-3.

Navarro-Triviño, F. J., & Ruiz-Villaverde, R. (2020). Allergic contact dermatitis to eyeglass frame nosepiece caused by tetraethylthiuram disulphide and resorcinol monobenzoate. International Journal of Dermatology, 60(4), e156-e158.

REACH-reg. 2024a. Drometrizol. Registration Dossier - ECHA (europa.eu). Accessed June 2024

REACH-reg. 2024b. *p*-(1,1-dimethylpropyl)phenol. Registration Dossier - ECHA (europa.eu). Accessed June 2024.

REACH-reg. 2024c. Triethyl O-acetyl citrate. Registration Dossier - ECHA (europa.eu). Accessed June 2024.

REACH-reg. 2024d. Triethyl Citrate. Registration Dossier - ECHA (europa.eu). Accessed June 2024.

Shono, M., Numata, M., & Sasaki, K. (2018). Allergic contact dermatitis caused by Solvent Orange 60 in spectacle frames in Japan. *Contact dermatitis*, *78*(1), 83-84.

Shono, M., & Kaniwa, M. A. (1999). Allergic contact dermatitis from a perinone-type dye CI Solvent Orange 60 in spectacle frames. Contact dermatitis, 41(4), 181-184.

Šitum, M., Lugović-Mihić, L., Bulat, V., Peternel, R., Vojniković, B., Martinis, M., & Toth, I. (2013). Dermatological aspects of contact dermatitis from eyeglass frames and optical materials. Collegium antropologicum, 37(1), 19-24.

Sundhed.dk (2023). Growth curves for Danish boys and girls. Link: Growth curve, boys 0-20 years - The Patient Handbook on sundhed.dk ; Growth curve, girls 0-20 years - The Patient Handbook at sundhed.dk

Telang, G. H., & Brod, B. A. (1994). Allergic contact dermatitis to eyeglass frame nose-pieces. Journal of the American Academy of Dermatology, 31(1), 114-115.

Tsunoda, T., Kaniwa, M. A., & Shono, M. (2001). Allergic contact dermatitis from a perinone-type dye CI Solvent Red 179 in spectacle frames. Contact Dermatitis: Short Communication, 45(3), 166-167.

Xu et al. (2019). Effects of citrate ester plasticizers and bis (2-ethylhexyl) phthalate in the OECD 28-day repeated-dose toxicity test (OECD TG 407). Volume 172, 675-683. https://www.sciencedirect.com/journal/environmental-research" \o "Go to Environmental Research on ScienceDirect

Survey and risk assessment of chemical substances in spectacle frames
The objective of this project was to investigate the materials and potentially harmful substances that might be found in plastic spectacle frames, which can lead to allergic reactions like swelling and eczema. Through chemical analyses and risk assessments, the study also aimed to determine whether specific substances in plastic spectacle frames, across various price points, could pose a risk to children or adult users.

The project identified several concerning substances present in and migrating from the frames. The risk assessment revealed that two of the frames released significant amounts of o-acetyltriethylcitrate, likely acting as a plasticiser. This substance could potentially pose a risk for the development of allergies. The project also highlighted the difficulty in obtaining information about the presence of harmful substances in plastic spectacle frames.

The Danish Environmental
Protection Agency
Tolderlundsvej 5
DK - 5000 Odense C

www.mst.dk