Cosmetic product safety report.

L.Y.X. One-Step Gel Polish, 39669213.
55 colour shades.

2015-12-01
Eviderm Institute
Marie Lodén
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Introduction to the changes in the updates

The present report is an update of the previous reports dated 2015-02-20 and 2015-03-30. The updated parts since 2015-03-30 are marked in yellow. A further update was made 2015-11-30, marked in blue.

The updates include elementary data on the properties of the product, references to similar types of products/ingredients, and information on methods in performing safety assessments by other authoritative expert groups, such as the US based CIR (Cosmetic Ingredient Review Panel) and EU based SCCS (Scientific Committee on Consumer Safety). The undersigned Safety Assessor considers the majority of the added information as non-essential for this type of report, as it mainly focus on basic educational activities of the product and repetitions of information between the different sections in the report.

The added information also includes a brief review on the “three-step” nail polish from Depend and the issued sales ban and withdrawal from the market of this product, which has similarities with the present nail polish. This sales ban was not considered necessary to discuss in the previous versions, but only to briefly mention as the potential deficiencies of the banned polish were not considered to be applicable to the present product. Nevertheless, the information on the product and the actions taken by the MPA and the Nacka Land and Environment Court were integrated in the previous safety reports along with information from other data sources. This was covered using the following expression in the report: "No further data which could reverse the important assessment made by CIR has been identified in the literature since the publication of the CIR report."

The names of some searched data bases were given in the original report, but the list was not complete (2014-12-29), as no details on the method for the literature search are requested by the Commission regarding this type of product. If the search had been performed to elucidate e.g. the safety of medicinal products, then more information on the method had to be given, for example, the searched key-words, the actual searched data bases, and criteria for “acceptance – rejections” of the retrieved literature are to be presented.

The Safety Assessor considers expert group evaluations to constitute evidence at high level in the hierarchy of evidence and should be used if no conflicting data is available. This is also common practice in other scientific judgements (c.f. evidence based medicine) as well as in line with the Commission Implementing Decisions, a for example regarding the selection of a NOAEL value (3.8.6) "...if an opinion of the SCCS exists, the NOAEL used in the opinion should be used... if an opinion of another authoritative scientific committee exists, the NOAEL used in the opinion could be used, provided that the conclusions and limitations are applicable to the expected use." Hence, data from expert groups are preferred to data from single studies.

In the following, the changes made to the original report are marked in yellow or in blue, to facilitate judgement of the added information. No data from the original document has been removed or changed.

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A. Cosmetic product safety information

Responsible Person: L.Y.X. Cosmetics AB, Allévägen 38, Tungelsta Box 104, 137 22 Västerhaninge, Sweden

Quantitative composition L.Y.X. One-Step Gel Polish, 39669213

<table>
<thead>
<tr>
<th>INGREDIENTS (INCI)</th>
<th>FUNCTION</th>
<th>CAS /EC</th>
<th>Interval or max%</th>
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<tr>
<td>POLYURETHANE ACRYLATE OLIGOMER (DI-HEMA TRIMETHYLHEXYL DICARBAMATE)</td>
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<td>947-19-3/213-426-9</td>
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</tr>
<tr>
<td>CI 77891</td>
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</tr>
</tbody>
</table>

Physical/chemical characteristics and stability of the cosmetic product

L.Y.X. One Step Gel Polish is a monophasic UV-light curable polish for nails. The physical/characteristics of the ingredients are briefly described below along with the toxicological profile of the ingredients. Additional information is to be found in other parts of the product information dossier.

Further information on the function of the product, the polymerization process and other typical use of this type of ingredients are found in the literature cited in the Toxicological profile of each of the ingredients (see below), where e.g. the data in the CIR-report provides the reader with further sources of literature on monomers and their curing. Also searches on the internet will provide the interested party with more in-depth information. The company has also repeatedly expressed its willingness to present the product to the Medical Product Agency and discuss various aspects of its function in more detail, without success. The scope of the present Cosmetic Product Safety Report is not to discuss the curing process in detail, but a simple figure showing the curing process when a liquid formulation is activated with a UV-sensitive photoinitiator is given below.
Typically the photopolymer consists of a mixture of multifunctional monomers and oligomers in order to achieve the desired physical properties. Therefore a large variety of monomers and oligomers have been developed that can polymerize in the presence of light (e.g. UV, LED) to reach the desired hardness, flexibility, colour, gloss etc. More information on industrial coatings, e.g. for cars and graphic arts, can be found in a supplier brochure, also describing the use of the present photoinititor.\(^8\)

The finished cosmetic product is a colored and almost odorless liquid, for more information see product information file. The stability of the cosmetics product has been investigated using standard techniques for cosmetic products and found to be adequate under reasonably foreseeable storage conditions. The Period After Opening (12 M) is labeled on the product.

**Microbiological quality**

The product is water-fee and does not allow growth of microorganisms.

**Impurities, traces, information about the packaging material**

The packaging is suitable for its use. The purity of the colours is reported to be at the highest standard possible and those with purity restrictions for food use are also manufactured to be used in food.

The container is a standard white glass container with plastic applicator made of polypropylene and polyethylene. The polypropylene part fulfils the harmonized requirements on materials used for articles or components of articles intended to come into contact with food as described in the European Directive 2002/72/EC and other appropriate directives.\(^c\) The LDPE part of the applicator complies with the applicable restrictions set by the REACH Regulation (CE) No 1907/2006, annex XVII “Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles” and following amendments, including Regulation (CE) No 552/2009. The Riblene is a Low Density Polyethylene (LDPE), produced with approved components (monomer, additives, etc.) under a third party certified ISO 9001:2008 Quality Management System.\(^d\)

**Normal and reasonably foreseeable use**

L.Y.X. One-Step Gel Polish, 39669213, is packed in a 5 and 10 ml containers. The users of the product is carefully instructed to use the product on the nails and to prevent the skin to be exposed to the polish (L.Y.X. One Step Gel Polish Instruktioner). It is stated on the container that exposure to the skin could induce irritation and it is stated in the package leaflet that overdosing should be avoided to prevent excess product to contaminate the skin. Further, it is stated that excess product close to the skin should be removed. Furthermore, it is labelled on the container that contact with the eyes should be avoided. A thin layer of the product should be applied to the nails which then is hardened for 30 s under a LED lamp. The LED lamp promote polymerization. Thereafter a second layer can be applied which is hardened for 60 s beneath the lamp. The nails are treated separately (one or two at a time) to facilitate the curing process beneath the lamp. This procedure will reduce

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\(^c\) Total Petrochemicals Research Feluy, December 7, 2009. Polypropylene PPH 10099 grade as produced in Europe.

\(^d\) Versalis, Italy. Product stewardship regulatory statement. Revision May 21, 2012
the risks for inadvertent exposure to non-hardened nail polish. The users are also instructed not to overdose the polish, to prevent contamination on the surrounding skin.

The possibility of secondary exposure to the product (e.g. inhalation and ingestion) is unlikely or negligent. Furthermore, it is not likely that the product is used on the teeth, in the mouth or on other mucous membranes, for example in the intimate region. The product presentation does not mimic the presentation of food, which reduces the risks for the product to be ingested. The product should be kept away from children, which is labelled on the container.

Exposure to the cosmetic product

There were no SCCS estimates on the daily exposure to the present type of nail polish, but in the recent update of the SCCS Notes of Guidance the amount per day was estimated to 0.04-0.05 g, based upon the frequency of use 1.17 times per week. The present product is reported to remain properly on the nails for 2 weeks, i.e. a less frequent application may be needed due to the high quality of the nail polish. A reasonable conservative estimate would be 2 mg per sq cm once a week, i.e. ca 20 mg (10 nail plates x 2 mg/cm²), which would be roughly 0.05 mg/kg bw/day (20 mg / 60 kg bw / 7 days = 0.047). Hence, the previous estimate on the daily exposure of the present product is in accordance with the newly proposed data in the SCCS Notes of Guidance. The normal and reasonably foreseeable use of the product is considered not to exceed this exposure. However, it might be argued that this dose is an overestimation, as the exposure is based upon once-weekly application and not application every two weeks, which is recommended in the product leaflet. Furthermore, the estimated amount per application may be an overestimation, as this dosing gives a fairly thick layer of this particular liquid which does not contain any volatile organic solvents. Larger amounts may be applied topically without this layer being sticky if the applied product contains high concentrations of volatile ingredients, as such ingredients (e.g. water, alcohol) rapidly evaporate and leave a much thinner film on the outside of the body. It should of course be remembered that the nails usually is larger than 1 sq cm, but 1 sq cm is the area of the nail plate in contact with the skin.

Exposure to the substances

The relative daily exposure (mg/kg bw/day) of each ingredient can be calculated from daily exposure, the bioavailability and the concentration in the product. The bioavailability and systemic exposure is not known, but the penetration via the nail is usually considered negligible. Furthermore, lateral diffusion of the ingredients from areas outside the nail plate, which is not in contact with the skin to the nail plate in contact with the skin, is considered to be nil. The EU Commission Guideline does not discuss penetration via different parts of the nail plate, but states that “Absorption can occur through several external routes: dermal, oral and inhalation”. Thus, ungual absorption is not mentioned and hence may not need to be further discussed in safety reports, unless the ingredients are highly toxic or exert other banned properties, such as CMR (see discussion on TPO in the Reasoning section below).

In the table a typical exposure to the ingredients is given; in this case represented by the example colour shade no 5.

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Eviderm Institute AB, www.eviderm.se

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SCCS (Scientific Committee on Consumer Safety), SCCS Notes of Guidance for the Testing of Cosmetic Ingredients and their Safety Evaluation 9 th revision, 29 September 2015, SCCS/1564/15
Safety Report, L.Y.X. One-Step Gel Polish, 39669213, No of shades: 55.

**INGREDIENTS (INCI)**

<table>
<thead>
<tr>
<th>INGREDIENTS (INCI)</th>
<th>CONC %</th>
<th>Weekly applied dose (20 mg)</th>
<th>Topical exposure (mg) per kg bw and day (20 mg/60kg 7 d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DI-HEMA TRIMETHYLHEXYL DICARBAMATE</td>
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<tr>
<td>ETHYLENE GLYCOL METHACRYLATE. 2-Hydroxyethyl Methacrylate (HEMA)</td>
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<td></td>
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<tr>
<td>POLYMER ACRYLATE Oligomer</td>
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<tr>
<td>1-HYDROXYCYCLOHEXYL PHENYLKETONE, (1-Hydroxycyclohexyl) phenylmethanone (HYDROXYCYCLOHEXYL PHENYL KETONE)</td>
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</tr>
<tr>
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<tr>
<td>Total</td>
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<td></td>
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</tbody>
</table>

**Toxicological profile of the substances**

The toxicological profile of the ingredients in the cosmetic product is briefly summarized below, with particular focus on local toxicity evaluation (skin and eye irritation) and skin sensitisation. Further information, detailing MSDS, raw material specifications, certificates and other technical information is available in the Product Information File, stored at the manufacturer, or in the open scientific literature cited below.

**DI-HEMA TRIMETHYLHEXYL DICARBAMATE /HEMA /POLYMER ACRYLATE Oligomer**

In the present product DI-HEMA Trimethylhexyl Dicarbamate (Polyurethane Acrylate Oligomer, CAS 41137-60-4), HEMA (Ethylene Glycol Methacrylate. 2-Hydroxyethyl Methacrylate, CAS 868-77-9, EC 212-782-2) and Polymer Acrylate Oligomer (CAS 152187-46-7) are used as filmforming substances.

Methacrylate ester monomers are used as artificial nail builders in nail enhancement products, They undergo rapid polymerization to form a hard material on the nail that is then shaped. While Ethyl Methacrylate has been used as the primary monomer in nail enhancement products, other methacrylate esters are also used in the polymerization in the formation of cross-links to build the stiff layer.

CIR has evaluated the safety of methacrylates. The polymerization rates of methacrylate esters evaluated by CIR are within the same range as Ethyl Methacrylate. While data are not available on all of these methacrylate esters, the available data demonstrated little acute oral, dermal, or i.p. toxicity. In a 28-day inhalation study on rats, Butyl Methacrylate caused upper airway irritation; the NOAEL was 1801 mg/m3. In a 28-day oral toxicity study on rats, t-Butyl Methacrylate had a NOAEL of 20 mg/kg/day. Beagle dogs dosed with 0.2 to 2.0 g/kg/day of C12 to C18 methacrylate monomers for 13 weeks exhibited effects only in the highest dose group: weight loss, emesis, diarrhea, mucoid feces, or salivation were observed.

Butyl Methacrylate (0.1 M) and Isobutyl Methacrylate (0.1 M) are mildly irritating to the rabbit eye. HEMA is corrosive when instilled in the rabbit eye, while PEG-4 Dimethacrylate and Trimethylolpropane Trimethacrylate are minimally irritating to the eye. Dermal irritation caused by methacrylates is documented in guinea pigs and rabbits. In guinea pigs, HEMA, Isopropylidene-diphenyl Bisglycidyl Methacrylate, Lauryl Methacrylate, and Trimethylolpropane Trimethacrylate are strong sensitizers; Butyl Methacrylate, Cyclohexyl Methacrylate, Hexyl Methacrylate, and Urethane Methacrylate are moderate sensitizers; Hydroxypropyl Methacrylate is a weak sensitizer; and PEG-4 Dimethacrylate and Triethylene Glycol Dimethacrylate are not sensitizers. Ethylene Glycol
Dimethacrylate was not a sensitizer in one guinea pig study, but was a strong sensitizer in another. There is cross-reactivity between various methacrylate esters in some sensitization tests. Inhaled Butyl Methacrylate, HEMA, Hydroxypropyl Methacrylate, and Trimethylolpropane Trimethacrylate can be developmental toxicants at high exposure levels (1000 mg/kg/day). None of the methacrylate ester monomers that were tested were shown to have any endocrine disrupting activity.

These methacrylate esters are mostly non-mutagenic in bacterial test systems, but weak mutagenic responses were seen in mammalian cell test systems. Chronic dermal exposure of mice to PEG-4 Dimethacrylate (25 mg, 2 x weekly for 80 weeks) or Trimethylolpropane Trimethacrylate (25 mg, 2 x weekly for 80 weeks) did not result in increased incidence of skin or visceral tumors. The carcinogenicity of Triethylene Glycol Dimethacrylate (5, 25, or 50%) was assessed in a mouse skin painting study (50 microl for 5 days/week for 78 weeks), but was not carcinogenic at any dose level tested. The Expert Panel was concerned about the strong sensitization and co-reactivity potential of the methacrylate esters reviewed in this report. However, data demonstrated the rates of polymerization of these Methacrylates were similar to that of Ethyl Methacrylate and there would be little monomer available for exposure to the skin.

In studies addressed in the CIR-report, a cosmetician with a wide cross-reactivity to several different methacrylates, did not react to Di-HEMA Trimethyl Dicarbamate used in the present product. In the present product Di-HEMA Trimethyl Dicarbamate is used in a higher concentration than in the reported CIR assessment. Furthermore, Kanerva (1989) did not found any of 7 patients occupationally sensitized to dental resin products to react to Di-HEMA Trimethylhexyl Dicarbamate. Also Tucker (1999) reported data on 440 patients which suggest that Di-HEMA Trimethylhexyl Dicarbamate to have caused less contact allergy than other tested acrylates in the Chemotechnique series, as 2 of 268 patients elicited a positive response, where 29 or 337 elicited a positive response to HEMA. Polymers and oligomers are even less likely to diffuse into the viable tissue and cause unwanted reactions.

According to CLP HEMA is classified as:
- Eye Irrit. 2, H319 : Causes serious eye irritation
- Skin Irrit. 2, H315 : Causes skin irritation
- Skin Sens. 1, H317 : May cause an allergic skin reaction,
whereas Di-HEMA Trimethyl Dicarbamate is not classified as an irritant or a sensitizer.

In consideration of the animal toxicity data, the CIR Expert Panel decided that these methacrylate esters should be restricted to the nail and must not be in contact with the skin. Accordingly, these methacrylate esters are safe as used in nail enhancement products when skin contact is avoided.

Polymer Acrylate Oligomer is an already formed polymer with out any toxicological relevance in the present use. The harmlessness of the substance is further supported by other CIR reports, such as e.g. the one detailing the safety of Acrylates Copolymer and 33 related cosmetic ingredients. This type of ingredients function in cosmetics as e.g. binders, film formers and viscosity-increasing agents, as in the present product. CIR acknowledges the huge variation in the mix of monomers used in the synthesis of the polymer but conclude that these very large polymers are safe for use in cosmetic formulations when formulated to avoid irritation. The present product is not used on body surfaces where irritation may occur (e.g. on mucous membranes or on the skin). Furthermore, the harmonized classification of HEMA as an irritant signifies that it does not possess corrosive properties, neither on the skin, nor in the eyes. Another evidence of the non-corrosive properties, but instead a fairly low degree of irritation of both HEMA and Di-HEMA are the patch test concentrations used at dermatologic clinics to investigate potential allergy to the substances. This concentration is 2% for both ingredients.
HYDROXYCYCLOHEXYL PHENYL KETONE

Hydroxycyclohexyl Phenyl Ketone (1-Hydroxycyclohexyl Phenylketone, (1-Hydroxycyclohexyl) phenylmethanone) CAS 947-19-3, EC 213-426-9. The substance is a photoinitiator and is reported to function as a binding substance in CosIng. Data in Epa reports the oral acute toxicity rat to be 2895 mg/kg and at the substance to be irritating to the eyes. Noted classification as Eye Irrit 2 and Aquatic Chronic 1 in Echa. Furthermore, DNEL (Derived No Effect Level) is 21.16 mg/m^3 and the oral NOAEL is set at 300 mg/kg bw/day, as the oral administration of by gavage over a period of 3 months revealed no signs of systemic toxicity in male and female animals (rats) at dose levels up to 300 mg/kg bw/d.

CI 77510

CI 77510, Ferric Ammonium Ferrocyanide, is a synthetic blue pigment and allowed to be used in cosmetic products. The pigments must conform to the EU Regulation and be free from cyanide ions. The supplier conforms purity in accordance to EU Cosmetic Directive, which corresponds to the requirement of the Regulation.¹

CI 77742

Manganese violet, CI 77742 (CAS 10101-66-3), is an inorganic salt manganese ammonium pyrophosphate functioning as a colorant. The pigment is insoluble in water, whereas contact with strong alkali liberates ammonia. MSDS suggests irritation in eyes and in sensitive skin.² Manganese violet is approved as a colouring agent in EU and is also considered as safe by FDA for use in coloring cosmetics generally, including cosmetics applied to the area of the eye, in amounts consistent with good manufacturing practice.³ The present quality is manufactured for use in food, drug, and cosmetic applications and are produced to the highest purity standards possible.

CI 77891

CI 77891, titanium dioxide, is used to impart a whiteness to color cosmetics and personal care products that are applied to the skin (including the eye area), nails, lips, and it helps to increase the opacity, and reduce the transparency of a product formula. Titanium Dioxide absorbs, reflects, or scatters light (including ultraviolet radiation in light), which can help protect products from deterioration. Titanium Dioxide has a long history of use in body care products. CI 77891 may be used without restriction according to the purity requirements that have been established for the quality of the same material used in foods. The present quality conforms to the purity requirements and is manufactured for use in food, drug and cosmetics and are produced to the highest purity standards possible (SunChemical Corporation, C47-051 01.01.05)

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³ http://apps.echa.europa.eu/registered/data/dossiers/DISS-975e8192-4649-058b-e044-00144f6d031/AGGR-6055fbc6-7cc0-47e7-8aa2-91615da9f22a_DISS-975e8192-4649-058b-e044-00144f6d031.html#AGGR-6055fbc6-7cc0-47e7-8aa2-91615da9f22a, accessed 2014-12-25
⁴ C385410 PIGMENT BLUE 27. COLORANT MEETS ALL REQUIREMENTS OF US 21CFR, PARTS 70-82 AND EU COSMETIC DIRECTIVE 76/768/EEC, ANNEX IV, PART 1 AND AMMENDMENTS. SunChemical. PERFORMANCE PIGMENTS 5000 SPRING GROVE AVENUE CINCINNATI, OH, USA 45232
Titanium Dioxide is also allowed in EU to be used as a sunscreen active ingredient (25%) to protect against the adverse effects of ultraviolet radiation found in sunlight. The particles, irrespectively of size, are not considered to penetrate the skin and induce toxic effects.\(^4\)

**CI 17200**

CI 17200 (CAS 3567-66-6, D&C Red 33) is a red azo dye with mw 467. The color is listed in Annex IV (colorants allowed in cosmetic products) and may be used without restriction.\(^5\) As with other azo-colours it may be linked to discussions on adverse reactions when used at high concentrations in food.

**CI 15985**

The colouring agent CI 15985 (FDC yellow 6, E110, CAS 2783-94-0, EINECS/ELINCS 220-491-7) is a synthetic dye classed chemically as a monoazo color. The color is listed in Annex IV (colorants allowed in cosmetic products) and may be used without restriction when purity criteria as set out in Commission Directive 95/45/EC (E 110) is fulfilled. The present quality is supplied by the international company Sun Chemical Corporation and are manufactured for use in food, drugs and cosmetics and produced to the highest purity standards possible (MSDS C19-6619, 01.01.03/C70-5270 01.01.03).

**CI 15850**

CI 15850 (Pigment Red 57:1, Red 7 Lake 5281-04-9) / Disodium 3-hydroxy-4-[(4-methyl-2-sulphonatophenyl)azo]-2-naphthoate and its insoluble barium, strontium and zirconium lakes, salts and pigments (CAS 5858-81-1, EINECS/ELINCS 227-497-9, E180, D&c Red No. 6, pigment red 57) is classed chemically as a monoazo color. The color is listed in Annex IV (colorants allowed in cosmetic products) and may be used without restriction when purity criteria as set out in Commission Directive 95/45/EC (E 180) is fulfilled. The present quality from SunChemical Corp include U.S. Certified Organic Colorants, Purified Inorganic Colorants, and Non-Certified Organic Colorants, and are produced to the highest purity standards possible (Code C19-6619, 01/01/03).

**CI 77491, CI 77492, CI 77499**


These compounds are used as coloring pigments in a variety of applications. Iron oxides and iron hydroxides are produced synthetically and consist essentially of anhydrous and/or hydrated iron oxides. The range of hues includes yellows, reds, browns and blacks. Food quality iron oxides are primarily distinguished from technical grades by the comparatively low levels of contamination by other metals. Because some of the starting materials for synthetic Iron Oxide may come from the earth there may be trace amounts of heavy metals present. The levels of heavy metals in Iron Oxides are regulated by the FDA and EU, and the small amounts that may eventually be in cosmetic or personal care products do not pose a risk to human health. The following criteria is applied to iron oxides on cosmetics in EU (by total dissolution):

- Water soluble matter: Not more than 1,0 %
- Arsenic: Not more than 5 mg/kg
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- Barium: Not more than 50 mg/kg
- Cadmium: Not more than 5 mg/kg
- Chromium: Not more than 100 mg/kg
- Copper: Not more than 50 mg/kg
- Lead: Not more than 20 mg/kg
- Mercury: Not more than 1 mg/kg
- Nickel: Not more than 200 mg/kg
- Zinc: Not more than 100 mg/kg

The present raw materials are supplied by the international company Sun Chemical Corporation and are manufactured for use in food, drugs and cosmetics and produced to the highest purity standards possible (MSDS C33-5198 08.21.03 /C33-115 01.01.05/C33-8073 01.01.05/oxide 08.08.12, C33-5138 01.01.03).

**CI 77019**

Mica (CAS 12001-26-2, EINECS 310-127-6) (muscovite) belongs to the mica-group of earth minerals and typically contains 43-48% SiO2 and 30-36% Al2O3. Mica is used as an opacifier and to give products sparkle and shine. Mica based pigments are also approved as food additive. As it is obtained from natural sources it can be subjected to a sterilization process (by ethylene oxide) in order to reduce its microbiological content to an acceptable level. CIR Expert Panel has concluded that mica and other similar silicates are safe as currently used in cosmetic formulations.

**CI 77289**

Chromium hydroxide CI 77289 CAS 12001-99-9 is a mineral colorant Cr(OH)3 used in a variety of products. This ingredient contains trivalent chromium, a form of chromium that functions as an essential trace element in human metabolism. The pigment is allowed to be used in EU cosmetics and should be free from chromate ion. The present quality is manufactured by SunChemical Corporation and is produced to the highest purity standards possible (C61-6735 01.01.03).

**CI 77007**

This substance, named lazurite or ultramarine, is identified in the Colour Index by Colour Index Constitution Number CI 77007 (CAS 12769-96-9 / 1302-83-6 / 57455-37-5) as a mineral-derived blue pigment composed of sodium, aluminum, silicate and sulfate. Ultramarines may be produced synthetically.

**Undesirable effects and serious undesirable effects**

There are no reports on adverse skin reactions or other undesirable effects from the use of the present product. Since its launch, more than 25 000 containers of the product has been used in Sweden without any reports on undesirable effects. Instead case reports and customer feed-back suggest the product to be safer than similar nail polishes.

Nail hardeners have been supplied to the market in long term although some of have been shown to cause serious adverse skin reactions and been withdrawn from the Swedish market as is considered to pose a chemical risk due to a high amount of sensitizing acrylate monomer. However, it is not clear which monomer the withdrawal referred to and, for example, methyl

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http://www.fda.gov/ForIndustry/ColorAdditives/GuidanceComplianceRegulatoryInformation/ColorAdditiveListingRegulations/ListingofColorAdditivesExemptFromCertification/ucm108158.htm

metacrylate is not recommended by neither CIR, nor by FDA to be used in certain cosmetics for the nails. Furthermore, the withdrawn product had another composition and user instruction relating to the removal of non-consumed monomer using organic solvents after curing. The withdrawal and by MPA prohibited product had a much wider distribution and larger sales volume (>1 000 000 units) than the present “one-step” product. Fifty one complaints were reported to the Medical Products Agency (MPA), where the vast majority of complaints was received after broadcasting via the Swedish Television by the MPA and attention from other media on the potential risks using those products, where the Agency encouraged the customers to report complaints. Surprisingly, the Swedish authority did not further investigate the complaints, but took them as evidential support for the non-safe use of the cosmetic product and issued a European sales ban of this “three-step” product. This ban was in disagreement with the opinion of the Responsible Person and was not endorsed by other national competent authorities in Europe, see further details in documents at Nacka Land and Environmental Court. It may well be possible that some of the complaints were linked to, for example, nail diseases or other types of nail polishes, artificial nails or professional sculpturing of nails. For example, it is known that the lower molecular weight formaldehyde may be released from nail-enhancement products and cause allergic reactions. The professional treatments may also involve other type of chemicals (e.g. powders) which are mixed at site in nail saloons and then applied to the nails. The nails may also have been filed down, making the nail-plate and the skin more vulnerable to adverse reactions. It might also be worth noting that the German Authority (BfR) recommended the industry to voluntarily withdraw products from the market containing more than 80-90% of methyl methacrylate (the substance is not used in the present product and not approved as safe for use by CIR and FDA). Prior to the recommendation to withdraw the products the German Authority issued a scientific opinion on the risks using higher levels than 80-90% of methyl methacrylate in nail cosmetics. A similar scientific opinion has not been expressed by the Medical Product Agency on the present use of HEMA and Di-HEMA, but instead the Authority issued a sales ban of nail polishes containing these chemicals. Banning of HEMA and Di-HEMA is in conflict with the opinions of the Responsible Persons and appears not to be endorsed by international experts, FDA, or European Authorities other than the Swedish Authority.

It is emphasized in the Commission guidelines that adverse reactions should be collected and reported in a structured manner, and neither serious adverse reactions from cosmetics, nor high number of complaints will automatically result in a sales ban. Of importance for the risk management is the causality assessment, which aims to determine whether a notified serious undesirable event is considered to be attributable to the use of a cosmetic product or not. Five levels of causality is used from “very likely” to “excluded”. The Medical Product Agency did neither report any causality data or any other data on the composition of the banned “three-step” nail polish product (e.g. type of monomers, photoinitiator), nor any other data on received complaints on similar products evaluated by the Medical Product Agency. Absence of transparent reasoning regarding the ban of the “three-step” product was in clear contrast to the open scientific report made by the German Authority on the similar case in Germany. Hence, no data issued by the Medical Product Agency could be used to conclude that the present product suffered from the same potential deficiencies as the banned “three-step” nail polish. Consequently the conclusion made by the undersigned Safety Assessor was that the banned nail polished suffered from quality defects not applicable to the present product.

After its launch, the cosmetic product has been monitored by the responsible person, a distributor or relevant national authorities. This obligation arises from Articles 6 and 23 of the

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○ DOM M 4272-14 at Nacka Tingsrätt, Mark- och Miljödomstol


Regulation. If any serious undesired effects on consumer health appear, the relevant authorities will be informed about it without any delay and corrective measures will be adopted in accordance with the Regulation. At the same time, the responsible person will notify the Safety Assessor about this fact who will update the Cosmetic Product Safety Report based on the new findings and the adopted corrective measures.

Information on the cosmetic product

L.Y.X. One-Step Gel Polish, 39669213 has not been tested on animals, but similar products have been available for long on the market without any evidence of safety issues other than contact eczema if exposed to the skin. Furthermore, in a pilot study on 14 patients only one of the patients, previously diagnosed for allergic contact dermatitis due to exposure to polyphasic [ex-temporaneous mixtures with liquids and solid material during nail-building treatments] 3-steps gels, reacted with erythema and pruritus on left index finger after treatment with the present gel polish.\(^8\) Whether this reaction was attributed solely to the use of this “one-step” product was not firmly confirmed. Other Swedish case reports also suggest the current product to be safe for use in consumers with allergy to 3-steps nail hardeners without any evidence of adverse reactions after usages several times.\(^5\)

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\(^8\) Ventseslav Garow, Clinical Dermatology test, East Diagnostic and consultation center, Bulgaria, dated 14.01.2014  
\(^5\) Testperson A, började använda LYX One Step 9/12-2013, Testperson B, började använda LYX One step 12/210-2013, Testperson C; började använda LYX One Step 7/1-2014, Testperson D Började använda LYX One Step Gel Polish 22/1-2013.
B. Cosmetic product safety assessment

Assessment conclusion

The cosmetic product, including up to 55 different shades, assessed in the present report, L.Y.X. One-Step Gel Polish, 39669213, is considered to be safe for human health when used under normal and reasonably foreseeable conditions of use, taking into account the presentation, labelling and instructions for use (Article 3 of Regulation (EC) No 1223/2009).

Labelled warnings and instructions of use

There is no need to label any particular warnings and instructions of use in accordance with the regulation [Appendix III-VI]. However, the users are carefully instructed on how to use the product and that they should avoid exposure of the skin and the eyes. Furthermore, if the eyes are exposed to the product, then the eyes should be rinsed with water and a medicinal practitioner be consulted. The product should also be kept away from children.

The text on the container and in the package leaflet is satisfactory and in agreement with the present safety evaluation, see excerpts from the leaflet to the right. On the container it is stated (in English): “Warning: Excess exposure on the skin may give irritation on the skin. If contact with eyes, rinse immediately and contact a medicinal practitioner. Keep out of reach from children.” Furthermore, the symbol for package leaflet informs the users to also read the enclosed information.

In the enclosed package leaflet it can be noted that the consumers should use the product in one-step: “Everything in one step – Apply directly on the nail – Harden – Finish!” Then it is also stated in the leaflet that the “LED lamp is closed and hardens the L.Y.X. Gel Polish completely within 60 seconds.”

It is also stated that “Note: Prevent overdosing of the brush to reduce excess product to flow onto the skin. If needed, use L.Y.X. Multi-tool to remove excess product along the border of the nail or the cuticle.”

“Place the nails in the L.Y.X. mini LED lamp and harden for 30 seconds. 4. Apply a second layer of L.Y.X. Gel Polish and harden for 60 s."

As stated in part A, the instructions for use are available in the Product Information File and it has not been deemed necessary to attach the instructions for use or translate the text in the safety report. It is also stated in the Regulation that “The information contained in the product information file shall be available in a language which can be easily understood by the competent authorities of the Member State” (Article 11 §3), i.e. no translation to English is needed in Sweden having Swedish as the official language, as incorrectly stated by the Authority. However, the necessary warnings should be alerted in the report and then the Responsible Person should include the instructions and warnings in a satisfactory way on the product to facilitate the readability and understanding of the text. If it had been a medicinal product, then the text need pre-approval by the Authority prior to the launch, but this is not the case for cosmetics.
**Reasoning**

A larger number of nail polishes are available on the Swedish market. For example, 3318 different “nagellack” are marked in the web-shop named Lyko, out of which 312 is denoted as “gellack” which might be a suitable terminology for the present type of nail polish, where some varieties function as a “one-step” (e.g. Leyla) as the present product.

The present monophasic LED and UV-light curable nail polishes for adults (but kept away from children) are used to provide a hard colored layer on the nail plate. In total 55 number of different shades are evaluated, containing different proportions of the individual ingredients to achieve the desired cosmetic properties, such as e.g. viscosity and colour. Thus, the safety evaluation is made on concentrations which are allowed to vary ±5% without affecting the present reasoning and conclusion.

The formed layer on the nail plate is composed by reacting together the acrylate ester monomers in a suitable mix with pigments and polymer acrylate oligomer using a photoinitiator. The reaction is activated by the use of a light emitting diode (LED) lights, or equivalent light source. The present safety assessment is based on the use of a LED-lamp, specified to cure the polish. Also ordinary outside UV-light will harden the layer, as well as indoor light. This will take much longer time than the LED-light, but reduces contact to unreacted monomers if spill occurs. Without a proper curing and formation of a hard layer the product will not satisfy the consumer and would thus not be able to reach the market.

The Responsible Person has used the new technology (LED-lamp) and a new combination of ingredients, including the efficient photoinitiator, to improve the curing process. Thus, the current “one-step” product belongs to the new versions of improved nail enhancement products on the global market. Obviously HEMA and Di-HEMA has been used for centuries in nail enhancement products with e.g. UV-light to promote the exothermic reaction, otherwise no CIR report had been compiled. A large number of “three-steps”-products are also available on the global market (including Sweden and other European countries), where some also require the use of organic solvents to be fully functioning. No solvents are needed for the current range of colors.

The nail polishes do not contain any prohibited substances and there are no ingredients of human or bovine origin and none are classified as having Carcinogenic, Mutagenic or Reproductive (CMR) toxicity. The formulation is not prone to microbiological contamination, as it contains no water which can accommodate microorganisms.

The largest part of the ingredients in One Step Gel Polish are metacylate ester monomers (HEMA and Di-HEMA Trimethylhexyl Dicarbamate) commonly used in the present type of formulations and they have also been assessed by expert committees for consumer products (CIR), and found to be adequately safe. Presently, 171 products are reported to contain HEMA and 192 products to contain Di-HEMA in the voluntary EWG data base (Skin Deep) in the USA (October 2015).

The most important reference for the assessment - the CIR report (45p) - was published in the International Journal of Toxicology year 2005 and includes data from 147 references. Proper toxicological data on the important metacylate ester monomers and also the other ingredients (Hydroxycyclohexyl Phenyl Ketone [see references in the Toxicological Profile above], Polymer Acrylate Oligomer, Cl 15850, Cl 15985, Cl 17200, Cl 77007, Cl 77019, Cl 77289, Cl 77491, Cl 77492, Cl 77499, Cl 77510, Cl 77742 and Cl 77891) have been retrieved by careful data search in relevant data bases (e.g. PubMed, ToxNet, CosIng) and been obtained from the raw material suppliers (see data...
on the Toxicological profile of the ingredients denoted in Part A). The colour pigments are allowed to be used in the present type of product. No further data which could reverse the important assessment made by CIR has been identified in the literature since the publication of the CIR report.

In addition, data from the Medical Products Agency website and information from the court on the similar product Depend, which was banned for sale, have been considered (case Nacka TR M 4272). The purity of the ingredients and the packaging are satisfactory.

In the CIR report the rate of polymerization of a large number of monomethacrylates, dimethacrylates and trimethacrylates and ethyl methacrylate were discussed. Thermal data showed polymerisation 22 metacrylates at 50% to be within 5 min (Table 4 in the CIR-report\(^5\)). The present formulation with not less than 50% acrylates has a set time and maximum exothermic reaction shorter than 30 s, measured with a thermal imaging camera.\(^6\) The experimental study and characterisation of the change in temperature was used to illustrate the rapid exothermic reaction in one of the shades (no 39 Chasca)\(^7\), which is typical for the present range of the “One-step” nail polishes. The thermal camera is not routinely used in the development or quality control of the shades, as this is satisfactory done via tactile and visual evaluation. Not surprisingly the temperature of the studied layer returned to the ambient temperature at a slower rate than during subsiding of the exothermic reaction. This phenomena can be compared with lightening of a matchstick, which immediately becomes hot and then slowly returns to ambient temperature after consumption of the ignition material. In the present study the temperature was ca 3 degree Celsius higher in the layer 3 min after completion of the exothermic reaction compared to the degree before starting the reaction. A closer look of the temperature around the lamp suggest the entire material to potentially be slightly warmer due to the heat from the lamp (not measured).

In the ordinary product development process, the approval process of new different colour shades includes relevant tactile and visual evaluations of the formed layer. Failure to polymerise within the expected time are neither accepted by the company, nor by the consumers. Therefore a consistent hardening is a prerequisite for approval of each new formula. Hence, each colour shade is checked carefully and no significant differences in setting times have been observed between the different colour varieties. This is due to the fixed ratio of the ingredients in the vehicle, i.e. in the mixture without any colours. The level of photoinitiator is 6% in the vehicle, but will be lower in the actual product due to the addition of colours. Thus, the actual level of photoinitiator in the current range varies between 0%, but larger variations are allowed and the level is given in the composition, part A. Too low content of the photoinitiator will delay the curing process and may even leave a sticky surface on the nail. If the hardening of the polish should be incomplete deeper in the formed layer, then not only monomers but also the colours should be released from the nail polish and contaminate the skin and other material in close contact with the nails. Not only the contamination would be observed, but also unacceptable fading of the colour would be noticed. This should not be approved cosmetic properties of the product.

Hence, there are no data in the report that suggest the present composition to be more associated with increased risks, due to for example higher concentration of monomers such as e.g. Di-HEMA Trimethylhexyl Dicarbamate than reported to be found in other nail hardening products. Furthermore, the setting time, the formed non-sticky layer and the mechanical resistance of the layer strongly suggest the complete consumption of the monomers. High levels of unreacted monomers would give a sticky and non-resistant layer on the nail of the nail polish, which would result in a non-agreeable product with very limited possibilities to reach the market and the consumers. Furthermore, a minor residual amount of unreacted monomers in the layer will be trapped in the

\(^5\) http://apps.echa.europa.eu/registered/data/dossiers/DISS-975e8192-4649-058b-e044-00144f67d031/AGOR-6055fbc6-7cc0-47e7-8aa2-91615da9f22a DISS-975e8192-4649-058b-e044-00144f67d031.html#AGOR-6055fbc6-7cc0-47e7-8aa2-91615da9f22a, accessed 2014-12-25

\(^6\) SunChemical. PERFORMANCE PIGMENTS 5000 SPRING GROVE AVENUE CINCINNATI, OH, USA 45232

\(^7\) Chasca is composed of 5.5% photoinitiator, 59% HEMA and Di-HEMA, 28% polymer and the rest colors.
polymer matrix and reduce the chance of penetration through the nail plate. Furthermore, the nail plate is considered a formidable barrier to penetration, especially to lipophilic substances. In a recent chapter on ungual formulations and topical treatment of nail diseases in a book edited by the present Safety Assessor M Lodén M and Prof Hl Maibach (San Francisco) the nail structure and permeability are discussed by Kenneth A Walters (UK), (also enclosed). The author note that there is a difference between the permeability characteristics of the nail and the skin, which is related to the differences in lipid compositions between the two structures. Therefore, hydrophobic substances will encounter larger resistance to penetration than hydrophilic substances, especially if the substances also have larger molecules, such as e.g. Di-HEMA. Furthermore, Walters does not rule out the possibilities to treat diseases in the nail or below the nail plate, as penetration enhancers which opens up the structure can be used in the formulations. In the present product, no such enhancers are included. It can also be noted in documents referred to by the Medical Products Agency, that nail diseases can be treated with drugs, but the patients are instructed to remove the outer part of the nail plate mechanically to facilitate the absorption of the drug (e.g. see instructions for the treatment of yeasts, molds and dermatophytes with amolorfine; “the affected areas of nail (particularly the nail surfaces) should be filed down as thoroughly as possible using the nail file supplied. The surface of the nail should then be cleansed and degreased using a cleaning swab”). This clearly demonstrates the difficulties for substances to penetrate the nail. Furthermore, no organic solvents are needed to remove any uncured monomers on the nail in the present “one-step” product, as may be needed for the “three-steps” products.

The SCCS has expressed a similar opinion on the penetration of nail and trapping of ingredients in the polymer matrix in its assessment of a photoinitiator, abbreviated as TPO: “Human nail forms a formidable barrier for substances, for instance drug formulations topically applied for medical purposes. [...] TPO is used as a chemical photo-initiator for polymerisation of monomeric mixtures applied on the nail plate and most of it is consumed and chemically bound to polymer chains. After application of TPO containing gel to the nail plate, the UV-initiated polymerisation process can be considered as complete within about 2 – 3 minutes. TPO will be consumed rapidly during the polymerisation process. In the event that a minor residual amount will remain, it will be trapped in the rapidly hardened polymer matrix. This process reduces the chance of possible penetration through the nail plate or the accidentally exposed surrounding skin and thus, the systemic bioavailability can be considered as very low, if any.” Furthermore, of interest to the present assessment, the SCCS concludes that although TPO is considered a moderate skin sensitizer it is safe when used as a nail modelling product at a concentration of at maximum 5.0%. The careful evaluation of the photoinitiator TPO by SCCS and the cautious calculations of its Margin of Safety were necessary due to the classification of TPO as a CMR-ingredient. CMR ingredients are banned in EU-cosmetics and need to be actively approved prior to inclusion in cosmetics. Therefore, it was of utmost importance to preclude any risks for Reproductive toxicity due to absorption of TPO via the nail from nail polishes containing this substance. This is in sharp contrast to the ingredients in the present product which have no such banned properties and poses negligible risks for systemic toxicity, which is obvious from part A.

The calculated daily topical exposure to the nail polish is roughly 0.05 mg/kg bw. The Systemic Exposure Dosage (SED) of the ingredients can be used to compare this value with the Threshold of Toxicological Concern (TTC) or reported no observed adverse effects level (NOAEL); Despite absence of generally agreed values on chronic toxicity of all ingredients in the present product, the ingredients are considered to have Margin of Safety well above the necessary ratio (>>100), as the systemic exposure is almost negligible when the product is used as foreseeable. In a worst case

https://www.medicines.org.uk/emc/medicine/27934/SPC/Amorolfine+5++w+v+Medicated+Nail+Lacquer+[Arrow]/

x SCCS/1528/14 Opinion on the safety of Trimethylbenzoyl diphenylphosphine oxide (TPO).
scenario using the sum of both HEMA and Di-HEMA and taking ungual absorption as high as 20%, the Margin of Safety will be above 500 (based on the NOAEL and corrected with an extra factor of 3 for a 90 day study, 50% HEMA and Di-HEMA and 20 mg per week, bw 60 kg). If it is assumed that the monomers are consumed within 1 min and the amount of unreacted monomers are 1% (as estimated in the SCCS report on TPO), then the Margin of Safety will increase further (to >50 000).

A more detailed tabulation of the calculated Margin of Safety (MoS) for all ingredients (except for the colorants which are allowed in cosmetics products irrespectively of level, Annex IV EC Regulation) is given in the Table below. The necessity of making these calculations in such a detailed way is questioned, based upon the known toxicity of the ingredients and the impermeable nail plate. This is also emphasized by the SCCS (SCCS/1564/15); “If there is sufficient evidence that the dermal absorption of a cosmetic ingredient is very low, systemic exposure may be negligible and the calculation of a MoS may not be justified or applicable (see Sections 3.4.1.1 and 3.5.1). See also for example SCCS/1533/14.”

The NOAEL from part A is used along with generally agreed correction factors due to the length of the toxicity study. Hence, the NOAEL for the low molecular weight t-butyl methacrylate was reported to be 20 mg/kg/day (28 day, rat) and for the high molecular weight C12 to C18 methacrylate to be 200 mg/kg/day (13 weeks, dog). It might be argued that the dog NOAEL value should be used instead of the rat value for species consideration, and that the more similar chemical structure and longer test period would be more similar to the present substances, but as a worst case scenario, the more conservative and lower rat value is used in the calculations, as this appears to be more warranted in the present questioned report. Thus, the value from the rat study – 20 mg/kg/day – is divided by 3 to compensate for 28 days instead of 90 days exposure, i.e. the NOAEL is set to 6.7 mg/kg bw/day for the acrylates. (It can be worth noting that the harmonized classification of HEMA does not suggest the substance to exert other toxicities than irritation and sensitization, suggesting that 20 mg/kg/day might be an overestimation.)

The NOAEL for the photoinitiator is 300 mg/kg bw/day.

No value of the NOAEL is reported for the polymer acrylate oligomer, but it can be anticipated to resemble similar acrylate polymers which have been used for long time and been assessed by authoritative groups and found to be safe in cosmetics. The polymers are very large molecules and are generally harmless (c.f. dental implants, bone cement, contact lenses). Furthermore, the absorption via the nail is considered to be even less than the absorption of the monomers and consequently the risks for systemic toxicity is much less than for the monomers. Hence, assuming the extremely conservative values for both absorption and systemic toxicity, the Margin of Safety is calculated using the NOAEL for the monomers regarding both toxicity and absorption resulting in the final values for Margin of Safety as denoted in the Table below.

For clarity and readability, only values for one of the colours are given in the Table. It is obvious that higher level of the ingredients in the product will not jeopardize the The Margin of Safety (MoS). MoS is calculated by use of the following equation; MoS = NOAEL/ Systemic Exposure Dose. The Systemic Exposure Dose is calculated from the daily topical exposure and the absorption into the body. The agreed body weight 60 kg is used.

It is very obvious from the data in the Table that there are no risks at all for systemic toxicity of the nail polishes, irrespectively of composition and difficulties to assign penetration data or level of remaining unreacted monomer. The lowest MoS is 667 for Di-HEMA and the highest MoS is 100 000 000 000 for the photoinitiator, which far exceeds the requested value of 100, as also reported in previous versions of this safety report. Calculation of the MoS for nail products containing ingredients with low toxicity is therefore considered to be irrelevant and this interpretation is also in line with discussion in the SCCS Notes for Guidance and in the Commission recommendations, but in conflict with the MPA which argues that MoS should be calculated on all ingredients.

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* Rogiers V. To whom it may concern. June 15, 2015. Personal communication.
**INGREDIENTS (INCI)** | **CONC %** | **Topical exposure (mg) per kg bw and day** (20 mg / 60 kg 7 d) | **Systemic Exposure Dose (SED, mg/kg/day); 100% absorption of 50% non-reacted ingredients / 1% absorption of 1% non-reacted** | **NOAEL (mg/kg/day)** | **Margin of Safety (NOAEL/SED)**
---|---|---|---|---|---
DI-HEMA TRIMETHYLHEXYL DICARBAMATE | 42 | 0.02 | 0.01 / 0.000002 | 6.7 | 667 - 3350000
ETHYLENE GLYCOL METHACRYLATE, 2-Hydroxyethyl Methacrylate (HEMA) | 12 | 0.006 | 0.003 / 0.0000006 | 6.7 | 2233 - 11166666
POLYMER ACRYLATE OLIGOMER | 25 | 0.01 | 0.005 / 0.000001 | 6.7 | 1340 - 6700000
1-HYDROXYCYCLOHEXYL PHENYLKETONE, (1-Hydroxycyclohexyl) | 6 | 0.003 | 0.0015 / 0.0000003 | 300 | 200000 - 1000000000
CI 77510 | 2.6 | 0.001 | | | Annex IV
CI 77742 | 10.7 | 0.004 | | | Annex IV
CI 77891 | 2.3 | 0.001 | | | Annex IV
Total | 100 | 0.047 | | | 

Furthermore, a more frequent use of the nail polish will not reduce the Margin of Safety to unacceptable levels. Neither will any exposure to the skin outside the nails contribute to any systemic toxicity. Local skin reactions [contact eczema – irritation and/or sensitization] are considered to be more toxicological relevant than systemic toxicity from the use of the present formulation. It might be worth noting that metacrylates are used in other type of products in close contact or advertently places inside humans, such as for example in indirect food additives, drug delivery systems, contact lenses, dental technology.²

The stability of the ingredients is considered to be satisfactory in the container and no hazardous degradation products are expected to be formed during storage. Upon application of the product on the nails, the liquid will polymerize and form a hard surface within 20 s, but the polymerization will continue for another 40 s to complete the hardening of the product, as a safety measure if the polymerization was not complete during the first 30 s. The formed polymers themselves are typically safe, but traces of the reactive monomers may remain in the polymer and have been reported to be able to result in an adverse reaction, such as redness, swelling, and pain in the nail bed, among people who are sensitive to methacrylates. However, methyl methacrylate monomers are more frequently associated with these injuries than the acrylates found in the present product. It is also possible that the products which have caused adverse reactions have been used in a non-proper way, e.g. in combination with organic solvents or on nails which have been filed down prior to treatment with more aggressive monomers, such as methyl methacrylate. Methyl metacrylate is not used in the

The sensitizer properties of HEMA was also discussed by OECD in SIDS Initial Assessment Report 2001. Animal studies suggested HEMA to be a weak sensitizer in guinea pigs giving variable (mixed) results depending on the protocol. Positive reactions were shown only with injection of Freund’s adjuvant but not by topical application alone. Whether or not this chemical induces skin sensitization in humans were reported to be equivocal; mixed results are reported in the literature on dental clients. Based on human patch test results, HEMA was concluded by OECD to have sensitizing properties and to potentially cross-react with other (meth)acrylates.

This interpretation of the potential differences in sensitizing properties between acrylate monomers are also in agreement with a recent scientific overview which emphasized that contact allergens vary up to 5 orders of magnitude with respect to their relative skin sensitization potency and that differences between lower alkyl methacrylate ester are found. Furthermore, the authors conclude that lower alkyl methacrylate esters only possess weak skin sensitizing potency, as for example the most widely accepted predictive test Local Lymph Node Assay is negative for 2-ethylhexyl methacrylate and the EC3 values were never less than 40% for the other discussed alkyl methacrylate esters. These discussions are in obvious conflict with the opinion that HEMA is an “extremely potent allergen”, expressed by MPA without giving any data to this conflicting statement.

The access to the viable epidermis was also highlighted by the scientists as one factor which limits the skin sensitizing potency, in line with our reasoning about potential differences in permeability between HEMA and Di-HEMA and the reported positive patch test reactions. Furthermore, the fact that the products applied to the nails meet a formidable barrier in the nail plate and is restricted in their diffusion in the formed polymer matrix also significantly limit the risks for contact allergy. Ficks law of diffusion is reported to be as low as 0.15µg/cm² for methyl

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methacrylate in acrylic polymer product of the first 24 hr of contact at room temperature. Thus, without doubt, the diffusion constant for Di-HEMA and HEMA would be lower, thus reducing the risks for contact allergy to this nail polish to almost nil. Consequently, the prevalence of allergic contact dermatitis to HEMA and Di-HEMA from their use in the present type of “one-step” nail polish will be negligible based upon a) the low sensitizing potential of the ingredients, b) the favourable proportion of Di-HEMA to HEMA in the polish, c) the rapid and efficient consumption under the lamp and d) the extremely low permeability of potential residual monomers 1) in the polymer, 2) through the nail plate and 3) through the skin barrier.

The present type of nail-enhancement acrylate products has gained high popularity during the recent decades, and the internationally recognized dermatologist Prof An Goossens (expert in contact allergy) from Belgium commented on the high popularity and the few number of reactions to the product type: “a rather limited extend seen the enormous popularity of this type of products and the large group of users today” (see Prof Rogiers statement below).

The behavior of HEMA and Di-HEMA in the present nail polish gives clear evidence for their safe use, especially in combination with the suitable photoinitiator which rapidly turns the monomers into polymers under the LED-lamp. Even if the skin is contaminated with the product, no induction of allergy is likely to occur due to the inherent low risks for induction of allergy from the monomers.

The monomers and the other low molecular weight ingredients in the mixture may cause irritation when used on the skin or on mucus membrane if they are used without curing. But as the product is intended to be used on the nails followed by curing under the lamp, no in-depth discussions on the degree of irritation from the monomers are necessary in the present report. Further, there are no risks for irritation of the nails or the skin below the nail, due to the negligible penetration through the nail plate. In addition, as the product should not be used around the eyes, no further discussion on the degree of potential eye irritation is needed. The evaluation should be focused on the foreseeable use and instructions on inadvertent exposure are properly enclosed with the (to be used on the nails, avoid skin, remove from skin, not in the eyes, not for children etc).

The formed polymers and the polymer acrylate oligomer are even less likely to diffuse into the viable tissue and cause unwanted reactions and are therefore considered to be without toxicological significance, which is in compliance with CIR opinions on similar polymers on acrylates.²,³

It is concluded that sufficient information is obtained on the ingredients and the formulation L.Y.X Cosmetics One Step Gel Polish, 55 different shades, to be able to assess its potential risks to human health under normal and reasonable foreseeable use. Data on the ingredients capacity to induce systemic reactions or adverse skin reactions show absence of significant risks. However, like any cosmetic product that may be hazardous if misused, it is important that L.Y.X. One-Step Gel Polish, 39669213, carries the appropriate warnings and directions for safe use which also are applied to the product. One Step Gel should not to be used outside the nail plate but exposure to the skin, although not intended – may sometimes be inevitable in normal and reasonably foreseeable conditions of use. If the eyes are exposed they should be rinsed with water and medical attention should be sought. If inadvertently applied to the skin outside the nail plate, then the user will remove the product, which reduces the exposure time to the non-polymerized liquid. When the product is used on the nail plate and the instructions for use is followed, then the information gives no evidence that the product is will pose any risk to the consumers, despite its content of HEMA, Di-HEMA and other suitable ingredients and EC-approved colors. Instead the product can be expected to be well tolerated and only in rare circumstances induce reactions in sensitive individuals. Individuals with a known sensitivity to certain potential allergens (e.g. acrylate monomers) in the formulation may be at a higher risk. Furthermore, case reports and data from open studies also support the safety of the present formulation and suggest it to be less troublesome than similar products on the market.⁴

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² Ventseslav Garow, Clinical Dermatology test, East Diagnostic and consultation center, Bulgaria, dated 14.01.2014
Other open safety reports on similar one-step nail formulations also support the safety of the present types of product as it concludes that the nail polish “will give users the level of safety they can reasonably expect when used as directed”. The safety conclusion on the present product is also supported by independent safety statements issued by a Swedish Safety Assessor Ulf Åkerström (experienced in cosmetic product development and safety evaluations) and Prof Vera Rogiers who is the former co-chair of the EU Scientific Committee of Consumer Safety in the European community, and the rapporteur for the new SCCS Notes of Guidance and also is an internationally recognized expert for giving advanced training courses in the safety assessment of cosmetics. Vera Rogiers further substantiated her conclusion by reporting that she had contacted a world-wide expert in the field of sensitization (Prof An Goossens) and she reported that “Nail reactions have been also seen in consumers, but to a rather limited extent seen the enormous popularity of this type of products and the large group of users today.” This opinion further demonstrates that the improvement of this type of product that has been implemented by L.Y.X. Cosmetics by using a suitable proportion of monomers along with a safe photoinitiator which gives a rapid and efficient formation of a non-sticky and hard layer of the nail surface, most probably will reduce the risks of being sensitized, whereas the sales ban may have the opposite consequence.

Assessor’s credentials and approval

The present safety assessment has been carried out in accordance to article 3 of Regulation (EC) No 1223/2009 by the undersigned person, which has a diploma in pharmacy and toxicology. Furthermore the assessor is Doctor in Medicinal Sciences and Associate Professor in Experimental Dermatology. A copy of the references is also available within the Responsible Person.

After analysis of submitted information on the formulation and publicly available information of the toxicological profile of the ingredients, it is concluded that, according to the current state of scientific knowledge, the product is not expected to cause damage to the human health and can be marketed for the intended and foreseeable use as a cosmetic product. New scientific evidence and new regulatory opinions may change the conclusions made in the present assessment.

Eviderm Institute AB, Bergshamra Allé 9, SE-17077 Solna, Sweden.

Date: December 1, 2015

Signature:

General Notes

A Testperson A, började använda LYX One Stp 9/12-2013, Testperson B, började använda LYX One step 12/210-2013, Testperson C; började använda LYX One Step 7/1-2014, Testperson D Började använda LYX One Step Gel Polish 22/1-2013


BB To whom it may concern. Rogiers V. Vrije Universiteit Brussel, 2015-06-15. Personal communication.

CC CV Marie Lodén, see http://www.eviderm.se/startsida/curriculum-vitae-marie-lodn-254246
The product assessed in the present report must be manufactured in accordance with EU Guidance on Good Manufacturing Practice and comply with the relevant purity standards for cosmetic ingredients. It is assumed that the ingredients do not contain any undisclosed impurities/contaminants that would affect the conclusions reached.

The product must be in order to ensure that the cosmetic product safety report is kept up to date as required by Article 10(1)(c) of Regulation (EC) No 1223/2009, the safety of the finished product should be reassessed regularly. When changes in the legal requirements occur (e.g. restrictions of one of the substances included in the formulation), it should be checked, amongst others (e.g. labelling), whether the formulation still complies with the law, and the safety assessment should be reviewed and, if necessary, updated.

The safety assessment should also be reviewed and, if necessary, updated, where one or more of the following circumstances apply:

(a) new scientific findings and toxicological data on the substances are available which could modify the result of the existing safety assessment;
(b) changes occurring in the formulation or specifications of raw materials;
(c) changes occurring in the conditions of use;
(d) a rising trend in terms of the nature, severity and frequency of undesirable effects, both under reasonably foreseeable conditions of use and in the case of misuse.

In supplying this safety assessment Eviderm Institute makes no assurances that the individual raw materials are registered or exempt under REACH, which is usually not an issue if the substances are sourced within the EU. Importers into the EU of products containing any botanical ingredients derived from endangered species should also be aware of any restrictions in this field.

References
