COSMETIC PRODUCT SAFETY ASSESSMENT

HEMERA GEL LACQUER

Customer Reference:

Part B: Cosmetic Product Safety Assessment

CONFIDENTIAL

DELIVERED TO:

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Cosmetic Product Safety Assessment

Hemera Gel Lacquer

Customer Reference:

Product Information

A product to be used by adults intended to be applied on nails plates (client information). Predominant exposure would be to the nails and cuticle. Exposure to the skin, although not intended –may some-times be inevitable in normal and reasonably foreseeable conditions of use. Due to the nature of the product, exposure to the eyes, inhalation and ingestion is unlikely.

Formulation

See Appendix One for product formulation data

Assessment Conclusion

This cosmetic product is considered as safe under normal and reasonable foreseeable conditions of use. The ingredients are legally permitted as per Cosmetic Regulation (EC) No 1223/2009 and its amendments and the safety assessment has been carried out in accordance to Article 3 of this regulation. They must comply with the relevant purity standards for cosmetic ingredients. It is assumed that these ingredients do not contain any undisclosed impurities/contaminants that would affect the conclusions reached. The product must be manufactured in accordance with EU Guidance on Good Manufacturing Practice.

Under normal or reasonably foreseeable conditions of use, a product made to this formulation is unlikely to produce an abnormally high number of adverse reactions. The product will give users the level of safety they can reasonably expect when used as directed.

The toxicological data available on the individual substances and the end product, including all chemical and/or biological interactions and human exposure via intended and likely routes have been taken into account in this assessment. Whenever a NO(A)EL value is available for a specific substance, its Margin of Safety (MoS) has been calculated and taken into account. Where applicable, relevant systemic and local toxicity end points of the chemicals ingredients in this formulation have been considered as part of this risk assessment.

Labelling Warnings and instructions for use

Warnings

Keep out of reach of children.

Avoid contact with the skin and eyes.

Instructions of Use

As per manufacturer's instruction.

Fragrance Allergen Labelling

THERE ARE NO ALLERGENS WHICH ARE REQUIRED TO BE DECLARED ON THE PRODUCT LABEL AS PER ANNEX III TO COSMETIC REGULATION (EC) NO 1223/2009.

Reasoning

Product Toxicity Review

If used as directed, use of this product formulation should be uneventful in the majority of the general population.

Effects of the product as provided on the skin

The formulation as supplied may cause skin irritation especially if exposure is prolonged and/or repeated.

Repeated exposure to the formulation as supplied may produce allergy by skin contact.

Unlikely to cause damage to internal organs following absorption through the skin.

Exposure to this product is unlikely to result in phototoxic effects.

Effects of the product as provided on the eye

Eye contact is unlikely to occur during normal use.

Accidental exposure of the eye to the formulation as supplied may result in eye irritation.

Effects following ingestion of the product as provided

Ingestion is an unlikely route of exposure.

The formulation as supplied if swallowed is likely to cause irritation to the mouth and upper digestive tract.

Effects following inhaling of the product as provided

Inhalation is an unlikely route of exposure.

Ingredient Toxicity Review

Most of the ingredients are widely used and have history of safe use in humans. Acrylates copolymer is a copolymer of two or more monomers consisting of acrylic acid, methacrylic acid, or one of their simple esters. It has been reviewed by CIR expert panel and considered safe for use in cosmetics at the level used in this product when formulated to avoid irritation. Bumetrizole is an organic compound that has been approved by US FDA to be approved as indirect food additive. As per ECHA, it has low potential for acute toxicity, eye irritation, skin irritation and skin sensitisation. Therefore, at the level present in this formulation it is unlikely to cause any safety concern.

HEMA (2-Hydroxyethyl Methacrylate) causes skin irritation, causes serious eye irritation & is a skin sensitizer. It has been reviewed by CIR expert panel under the group of Methacrylate ester monomers and considered safe as used in nail enhancement product when skin contact is avoided. According to CIR report, product containing these ingredients should be accompanied with directions to avoid skin contact, because of the sensitizing potential of methacrylates. Given that this is a nail care product and the normal nail plate acts as a good barrier to penetration of chemical substances in general. This leaves very little chance for the monomers to be absorbed in any appreciable amount through the nail plate. Exposure to the eyes is unlikely. Exposure to the skin is not the intended use of the product albeit sometimes inevitable. The following warning is recommended: *Avoid contact with the skin and eyes.* HEMA has also recently been reviewed by SCCS and considered safe at up to 35% when used in topically applied UV-cured artificial nail modelling systems (SCCS/1592/17).

Colorants used in this formulation have low order of toxicity. Mica (CI 77019) is considered to be chemically inert and has low acute toxicity. It is not considered to be irritating to the skin or eyes and not known to cause skin sensitisation or elicitation of allergic reaction. Titanium dioxide (CI 77891) is a naturally occurring mineral. FDA lists titanium dioxide as a color additive used in coloring products, including cosmetics and personal care products applied to the lips, and the eye area, provided it meets certain specifications. Titanium dioxide is also an approved colorant for food, drugs and medical devices. FDA includes titanium dioxide on its list of indirect food additives. Colorants (CI 77891, CI 77499, CI 74160, CI 77492 and CI 77491) used in the formulation are listed under Annex IV of EU cosmetic regulation 1223/2009. The supplier has stated that the colorants used in the formulation meets the requirements of Regulation (EC) No.1223/2009 for cosmetics, and those colorants requiring food grade purity criteria meets the requirements of Regulation (EC) 231/2012.

As a leave-on product, repeated and long-term exposure is expected albeit limited systemic exposure is anticipated. Due to nature and/or the expected exposure levels of the ingredients, the formulation is expected to be of low systemic toxicity. Therefore, significant systemic toxicity is not expected in the short, medium or long term with repeated exposure to the product under normal and reasonably foreseeable use. Where adequate data is available, a Margin of Safety (MoS) has been calculated to be > 100, thus supporting the safety of the ingredient as formulated in this product.

Overall, taking into account the intended application, frequency of exposure and, the toxicological profiles of the individual ingredients as well as the supplier ensuring that the ingredients are of high purity, the product is not expected to cause damage to human health in the short, medium or long term under normal and reasonably foreseeable conditions. Although it cannot be totally discounted that a few susceptible individuals may experience allergic or other idiosyncratic reaction with the product particularly if already sensitised to one of the ingredients.

Margin of Safety Review

Where a NOAEL is available for a chemical ingredient that is considered as a toxicological concern, the Margin of Safety (MoS) has been calculated as greater than 100 taking into consideration any known data on dermal absorption and bioavailability. It is generally accepted that the MoS should be a least 100 to declare a substance safe for use in a finished product and the safety of this formulation is further supported by this uncertainty factor.

See Appendix One for a toxicological review of the formulation ingredients

Exposure Scenario

Product Class: Nail and cuticle products	**IFRA Category:** Category 8
Product Subclasses: Other nail and cuticle products, Other nail and cuticle products,	**Product Group:** Other nail and cuticle products
Product Group: Cosmetic	**Part of body exposed to undiluted**: Apply on nails
Product Name: Hemera Gel Lacquer	
Targeted Population: Adult	
Amount per application (g): 0.3	**Number of applications per day**: 2-3 times per week
Physical Form: Liquid	**Total Amount applied per day (g)**: 0.05
Skin Surface Area of Application (cm^2): 4	**Amount per Unit Area of Skin per day ($mg/cm^2/day$)**: 12.5
	Estimated Daily Exposure (mg/kg/day): 0.833
Exposure Time Neat: 3360 min, 156 x / year	**Retention Factor**: 1
Exposure Time Dilute: Not Applicable	
Exposure Time Solvent Inhalation: Inhalation - 5mins. Inhalation rate: 23.1 litres/min	**Exposure Time Aerosol Inhalation**: Not Applicable

Fragrance Composition

This formulation does not contain a synthetic fragrance and therefore a fragrance safety evaluation as per IFRA code of practice is not applicable to this product.

Microbiological Quality

Microbiological specifications:

To comply with the EN ISO 17516:2014 standard for Cosmetics — Microbiology — Microbiological limits, the following maximum limits apply:

Category 2: Other cosmetic products.
Total Aerobic Mesophilic Microorganisms (Bacteria plus yeast and mould): ≤ 1000 cfu/g or 1000 cfu/ml of the product. Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus and Candida albicans must not be detectable in 1 g or 1 ml of the cosmetic product.

The microbiological specifications for the product have been supplied and based upon the conclusions therein, meet the minimum industry requirements specified in European Standard EN ISO 17516:2014 Cosmetics – Microbiology – Microbiological limits for cosmetic products.

Ref.: MICROBIOLOGY QUALITY ANALYSIS TEST REPORT, 19/01131/02 - Hemera Gel Lacquer, Date: 25 February 2019
Microbial Limits Test Report, Hemera Gel Lacquer, Date: 19-Feb-19

Preservative challenge test:

The efficacy of the preservation of a cosmetic product has to be assessed experimentally in order to ensure microbial stability and preservation during storage and use.

The preservative efficacy test results for this product have been supplied and based upon the conclusions made therein appear to meet the industry standard requirements specified in ISO 11930:2012 (E), Cosmetics — Microbiology — Evaluation of the antimicrobial protection of a cosmetic product.

Ref.: Preservative Efficacy (Challenge) Test –ISO 11930:2012, Hemera Gel Lacquer, Date: 02/04/2019
PRESERVATIVE EFFICACY (CHALLENGE) TEST REPORT ISO 11930:2012, Hemera Gel Lacquer, Date: 10 April 2019

Property	Method	Specification
Aerobic Mesophilic Bacteria		<10 CFU/g
Yeasts and Moulds		<10 CFU/g
Pseudomonas aeruginosa, Candida albicans, Escherichia coli, Staphylococcus aureus,		Absent

Product Stability

The physical stability of the finished product should be established, ensuring that no changes in its physical state

occur during transport, storage or handling of the product. To make sure that no stability problems are induced by the type of container and packaging used, physical stability tests should be carried out with inert containers and those intended to be used on the market.

It is assumed that the responsible person has selected all pertinent criteria required to evaluate the stability of this cosmetic product during reasonable foreseeable conditions of storage.

The stability report has been provided by the supplier and based upon the conclusions made therein, this cosmetic product appears to be stable under reasonably foreseeable storage conditions.

Ref.: Cosmetic Stability Report, Hemera Gel Lacquer, Date: 04/06/2019
Stability Test Report, Hemera Gel Lacquer, Date: 06/06/2019

Packaging Material Information

It is assumed that the responsible person has identified the most applicable testing required to determine the packaging stability and its interaction with the cosmetic product contained within it. Taking into consideration the information supplied to the assessor, there appears to be no immediate health concern due to the grade and characteristics of packaging materials in direct contact with the final product.

Impurities/Traces/Prohibited Substances

Where the specification is provided it is noted that this product does not contain any impurities at levels likely to cause harm to the user. The purity specification of the raw material ingredients have been reviewed where they have been provided by the supplier at the time of assessment. It is found that the raw materials do not contain any prohibited ingredients listed in Annex II to Regulation (EC) No 1223/2009 at concentration likely to cause harm to the user when used as directed under normal and reasonably foreseeable conditions of use.

Presence of Nanomaterials

In accordance to Cosmetic Regulation (EC) No 1223/2009, a nanomaterial is an insoluble or biopersistant and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm.

The supplier has confirmed that this cosmetic product does not contain any nanomaterials that are known to them with the meaning of the definition as stated in Cosmetic Regulation (EC) No 1223/2009.

Serious/Undesirable effects

The following data of the serious undesirable effects and/or undesirable effects have been supplied at the time of assessment and these are detailed below.

The manufacturer has clarified that this product has been introduced into the market recently. Therefore, there is no known undesirable effect and/or serious undesirable effect data.

Ref.: Clarification statement, Date: 21 March 2019.

Specific Use Considerations

N/A

Assessor's Credentials and Approval of Part B

This product was evaluated by N. KACHHELA who is qualified by education, training and experience to evaluate the safety of cosmetic product formulations.

cosign

N. KACHHELA,M.S. Pharm (Pharmacology & Toxicology)
Intertek Health, Environmental & Regulatory Services (HERS)

Date: August 20, 2019

This product was reviewed by D. SANCHEZ CARVAJAL who is qualified by education, training and experience to evaluate the safety of cosmetic product formulations.

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D. SANCHEZ CARVAJAL, BSc (Veterinary), MSc (Toxicology)
Intertek Health, Environmental & Regulatory Services (HERS)

Date: August 20, 2019

Appendix One: Product Formulation Data and Toxicological Review of Ingredients

Formulation

The chemical names shown below refer to the raw materials used to formulate this product. The identity of the raw materials may be based on alternative nomenclature such as IUPAC name, Chemical name, INCI name or generic trade name. Furthermore, there may be instances where several CAS number exist for the same chemical ingredient. Where this has occurred, the most appropriate substitute will have been used where one has not been provided.

INCI Name	% Concentration	% Active	Activity in Product	CAS No	Chemical Name
ACRYLATES COPOLYMER	70	100	70	25133-97-5, 25035-69-2, 25212-88-8, 25086-15-1, 25035-69-2	ACRYLATES COPOLYMER
HEMA	20	100	20	868-77-9	2-HYDROXYETHYL METHACRYLATE
BUMETRIZOLE	5	100	5	3896-11-5	BUMETRIZOLE
CI 77891	3	100	3	13463-67-7, 1317-70-0, 1317-80-2	CI 77891 (TITANIUM DIOXIDE)
CI 77499	2	100	2	12227-89-3, 1317-61-9	CI 77499
CI 74160	2	100	2	147-14-8	CI 74160 (PIGMENT BLUE 15)
CI 77492	2	100	2	1332-37-2, 51274-00-1, 1345-27-3, 20344-49-4	CI 77492 (PIGMENT YELLOW IRON OXIDE)
CI 77491	2	100	2	1309-37-1, 1332-37-2, 1317-60-8	CI 77491 (IRON OXIDE RED)
MICA	2	100	2	12001-26-2	MICA (CI 77019)

Toxicological Review of Ingredients

Chemical Name: Acrylates Copolymer			
Function: Film former			
Regulatory Status (Toxicological Risk Assessment Report):			
Exposure	**NOAEL**	**Safety Factors**	**MoS**
ORAL	250 mg/kg bw/day	0	MoS For Adult: 1785.7

Summary Data:

Cosmetic Functions: Antistatic / Binding / Film Forming. Acrylates/C10-30 Alkyl Acrylate Crosspolymer is a copolymer of C10-30 alkyl acrylate and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters crosslinked with an allyl ether of sucrose or an allyl ether of pentaerythritol. They are produced from primary polymer particles of about 0.2 to 6.0 micron average diameter. The flocculated agglomerates cannot be broken into the ultimate particles when produced. Acrylates copolymers are used in many types of cosmetic products and have been evaluated by the Cosmetic Ingredient Review (CIR) Expert Panel which concluded that the acrylates copolymers are safe for use in cosmetics when formulated to avoid irritation of the skin. Acrylates copolymer is expected to be poorly absorbed and so has limited systemic bioavailability. The primary toxicological concern with acrylates copolymer is with the unreacted monomers and/or residual chemicals such as solvents, plasticisers or catalysts. Little residual monomers are generally present in acrylates copolymer; although residual acrylic acid may be as high as 1500 ppm, typical levels are reported to be 10 to 1000 ppm (CIR, 2002). The raw material grade of Acrylates/C10-30 Alkyl Acrylate Crosspolymer (Carbopol Ultrez® 20 Polymer; Lubrizol) according to the supplier's specification data contains <500 ppm residual acrylic acid, <0.45% residual solvent (cyclohexane and ethyl acetate) and < 1 ppm benzene (Lubrizol, 2010). The residual concentration of monomers in Acrylates Copolymers have been reported. According to the evaluation of reports "Ten companies representing the majority of the production of polymers sold for cosmetic use indicated that residual acrylic acid concentrations in polymers are typically between 10 and 1000 ppm, with an upper limit of 1500 ppm. One source reported Acrylates Copolymer can contain residual amounts of <=20 ppm ethyl acrylate, methyl methacrylate, methacrylic acid, and acrylic acid; another source reported that three samples analyzed using GC contained <0.2 to 0.8 ppm acrylic acid, 0.8 to 2.6 ppm methyl methacrylate, and 1.3 to 3.9 ppm ethylene glycol dimethacrylate. Additionally, it was reported to CIR that two polymers, both defined as Acrylates Copolymer, contained different residual monomers; the first contained 36, 20, and 45 ppm n-butyl acrylate, methyl methacrylate, and methacrylic acid, respectively, and the second contained 1500 and 200 ppm stearyl acrylate and methacrylic acid, respectively" (Final report on the safety assessment of Acrylates Copolymer and 33 related ingredients (Int J Toxicol Vol:21, Suppl 3 (2002) pp 1-50). The published toxicokinetics data for acrylic acid and methyl acrylate suggest that both may be absorbed through the skin, the gastrointestinal tract and nasal cavity. Acute toxicity: Acrylates copolymer (~24% or 30% solids) has low acute toxicity with reported LD50 values of > 2 to 9 g/kg (rat) after oral dosing, and > 16g/kg (rabbit) following dermal application. The LC50 > 5.2 mg/L (rat, 4-hr) on inhalation exposure to the aerosol (MMAD: 1.4µm). However, acrylic acid has shown moderate toxicity on dermal application (LD50 – 295 to 950 mg/kg; rabbit). Irritation: The skin irritation potential of the polymer has been evaluated undiluted in rabbits according to international OECD Guidelines No. 404. The test material (0.5g of dry polymer, moistened with 0.5 ml distilled water) was applied to the intact skin and held in place under a semi-occlusive binder for an exposure period of four hours. Following the exposure period, the binder was removed, and the remaining test article was rinsed off the skin with the test sites subsequently examined and scored for dermal irritation for up to seven days following patch removal. Under the test conditions, the test material caused mild skin irritation (Primary Irritation Index 0.3). Likewise an eye irritation test with the polymer has been conducted. Undiluted and 5% solution was instilled in the conjunctival sac of rabbits and left unrinsed. The undiluted test material produced moderate corneal and conjunctival irritation (maximum mean score 37.7 out of 110; class 5 on a 1 to 8 scale) which was resolved within 21 days whilst at a concentration of 5%, minimal eye irritation was demonstrated (conjunctival; maximum mean score 9.3 out of 110; class 3 on a 1 to 8 scale) (Lubrizol, 2004). Thus, it is concluded that the acrylate copolymer has minimal skin and minimal to moderate eye irritation. Sensitisation: Acrylates copolymers did not produce a skin sensitisation reaction in series of guinea pig maximization test at challenge concentrations ranging from 5% to 75% following induction treatment with 0.5% to 25%. Mutagenicity/Genotoxicity: Acrylates copolymer was non mutagenic or shown

any evidence of genotoxicity in Ames tests, mouse lymphoma assays, in vitro chromosome aberration tests and in vivo bone marrow micronucleus test (CIR , 2002 and references cited therein). Repeat dose toxicity: No repeated dose toxicity data is available for the acrylate copolymer. Surrogate data with other structurally similar acrylic acid polymers are available. Oral and dietary administration studies with carbomers reported significant bodyweight reductions at high doses (5000 mg/kg/day) administered for 30 days. However, no effect on bodyweight gain was seen following administration of a carbomer in rat at 5% in diet (corresponding to ~ 4000 mg/kg/day) for 21 days; and in a 90-day study at 1% in diet (~ 800 mg/kg bw/d). In the dog, a no-observable-adverse-effect level (NOAEL) of ~ 250 mg/kg bw/d (i.e. 1% in diet) was reported. Acrylates copolymer (polymer backbone was n-butyl acrylate, methyl methacrylate, methacrylic acid) formulation containing 69% ethanol was tested for inhalation toxicity in rats exposed whole-body for 13 weeks to 1, 10, or 30 mg/m3. The actual concentrations of polymer that the animals were exposed to were 0.185, 1.67, and 4.94 mg/m3 (CIR 2002 and references cited therein). No significant exposure related lesions or changes were noted and the formulation was concluded as having a relatively low pulmonary toxicity with the no-observable-adverse-effect level (NOAEL) of 10 mg/m3 of the formulation (corresponding to 1.67 mg/m3 acrylate copolymer). Acrylic acid monomer had no adverse effects on rats in a 12-month drinking water study at daily mean intake of 9, 61, 140, and 331 mg/kg bw/d; respectively. Sodium polyacrylate was concluded not to show teratogenicity or embryotoxicity in the rat at oral doses of up to 1125 mg/kg bw/d (high molecular weight material, 90000 Da) or 3000 mg/kg bw/d (low molecular weight material, 4500 Da). Maternal toxicity (3 deaths) was noted at 1125 mg/kg bw/d (high molecular weight sodium polyacrylate). Repeated dermal application in the mouse for 13 weeks using 0.1 ml volumes of acrylic acid monomer reported 1% concentration to be well-tolerated (McLaughlin et al. 1995 as cited in CIR, 2002). Acrylic acid administered at dose levels of 83, 250, or 750 mg/kg acrylic acid in the drinking water daily to rats in a 2-generation study reported a NOAEL of 250 mg/kg. IARC (1999) concluded that “acrylic acid is not classifiable as to its carcinogenicity to humans”. “Read across” to data on carbomer provide the lowest NOAEL of 250 mg/kg bw/d. Photo-induced toxicity: No data available indicating phototoxicity potential. Other data (human): Human repeated insult patch test (HRIPT) has been conducted with the polymer material. 150 mg of a 10% distilled water paste of the polymer material was applied to the skin of 113 human volunteers and the skin irritation and sensitisation potential was assessed. The test material did not produce any evidence of skin irritation or skin sensitization under the conditions of the test (Lubrizol, 2004). Dermal / percutaneous absorption: No data on dermal absorption is available for the copolymer. However, absorption of the monomer, acrylic acid, has been reported to be 24% of dose following application to rat skin samples in vitro with approximately 60% of the dose evaporating on application (Black et al. 1995). Hence, the dermal absorption of acrylates copolymer is expected to be less than 24% of the applied dose. Margin of Safety: NOAEL: 250 mg/kg bw/d; Dermal Absorption (Dap) = 24 % References: Lubrizol 2004: Carbopol Ultrez 20 Polymer Toxicology studies. Noveon Consumer Specialties Toxicology and Microbiology studies; TOX-080, February 5, 2004. Available at: http://www.lubrizol.com/PersonalCare/Products/Carbopol/CarbopolUltrez20.html CIR 2002: Final report on the safety assessment of acrylates copolymer and 33 related cosmetic ingredients. International Journal of Toxicology, 21 (Suppl. 3): 1-50, 2002. Accessed at: www.cir-safety.org

Chemical Name: 2-Hydroxyethyl Methacrylate

Function:HEMA is used film forming agent in cosmetics.

Regulatory Status (Toxicological Risk Assessment Report):

Exposure	NOAEL	Safety Factors	MoS
ORAL	30 mg/kg	0	MoS For Adult: 180

Summary Data:

Cosmetic Function :Film Forming. As supplied classified as irritating to skin and eyes along with a skin sensitiser. The extent and time of exposure to this substance must be minimised. CIR Concludes, safe in nail enhancement products when skin contact is avoided; products containing this ingredient should be accompanied with directions to avoid skin contact because of the sensitizing potential of methacrylates. CIR 2005 Methacrylate ester monomers are used in 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 is the primary monomer used in nail enhancement products, other methacrylate esters are also used. This safety assessment addresses 22 other methacrylate esters reported by industry to be present in small percentages as artificial nail builders in cosmetic products. They function to speed up polymerization and/or form cross-links. Only Tetrahydrofurfuryl Methacrylate was reported to the FDA to be in current use. The polymerization rates of these methacrylate esters 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, Isopropylidenediphenyl 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 crossor 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 exposure to the skin. 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. CIR maximum use concentration in nail products is 30%.

Chemical Name: Bumetrizole

Function:U.V. absorbers

Regulatory Status (Toxicological Risk Assessment Report):

Exposure	NOAEL	Safety Factors	MoS
		0	MoS For Adult:

Summary Data:

A UV absorber used to protect the colours. As supplied minimally irritating to skin and eye. High LD50 value >5000mg/kg. Not a skin sensitiser. At typical levels of use unlikely to cause irritation or allergy.

Chemical Name: CI 77891 (Titanium Dioxide)

Function: Colour

Regulatory Status (Toxicological Risk Assessment Report):

Exposure	NOAEL	Safety Factors	MoS
ORAL	2500 mg/kg bw/day	0	MoS For Adult: 19998400.1

Summary Data:

Function: Colourant, opacifying/uv absorber. Titanium dioxide may be in the anatase or rutile form. It is an approved food color (E171) with an unspecified acceptable daily intake. Bioaccessibility data on titanium released from titanium dioxide were determined when exposed to synthetic biological media of varying pH and composition. Only a small fraction of titanium was released / dissolved from the titanium dioxide powder during exposure to any of the media matrices of varying acidity and composition. A trend with somewhat higher release rates with increasing acidity and exposure period was evident. Not classified in the EU. Titanium dioxide (dust) is classified by IARC as Category 2B, ''Possibly carcinogen to humans'' (IARC, 2010). Food and Drug Administration (FDA) has authorized the use of titanium dioxide in food, in general, at a limit not to exceed 1% by weight of the food. It has approved the use of titanium dioxide for use in OTC sunscreen drug products at concentrations up to 25%. Acute toxicity: Not acutely toxic or harmful by the oral, inhalation or dermal route. Acute oral toxicity studies in animals (rats or mice) with micro/non micro crystalline/coated/uncoated forms of titanium dioxide were conducted, in general, the LD50 >5000 mg/kg bw. The dermal LD50 for rats is determined to be >2000 mg/kg bw (SCCNFP, 2000). The inhalation LC50 in rats was > 2 mg/L (4 hour exposure). Irritation: Non-irritating. Results of different skin irritation studies with various types of titanium dioxide showed varying degree of erythema and completely recovered at 72 hours after application. Results of animal studies demonstrated that coated and uncoated titanium dioxide is non-irritating to the eye (SCCNFP, 2000). Sensitisation: No sensitisation was observed with both coated and uncoated titanium dioxide in both animal and human studies. Mutagenicity/Genotoxicity: In vitro and in vivo studies indicate that titanium dioxide is non mutagenic or genotoxic. It was negative in a battery of standard assays. Repeat dose toxicity: Results of subchronic feeding study in mice with anatase titanium dioxide demonstrates that it has no specific systemic effects. Titanium dioxide administered by oral gavage at a dose level of 24 g/kg bw/d to rats for 28 days showed no adverse effects (REACH Dossier). Benign tumours (bronchioloalveolar adenomas and cystic keratinising squamous cell carcinoma) were reported in a 2-year inhalation study in rats at 250 mg/m3. The NOEC (No observed effect concentration) for non-neoplastic changes was reported as 10 mg/m3. Titanium dioxide administered in the diet at doses of 25000 (~1250 mg/kg bw/d) or 50000 ppm (2500 mg/kg bw/d) to rats for 2 years showed no treatment-related increased in tumour incidence or any systemic toxicity effects. NOEL was > 2500 mg/kg bw/d. Photo-induced toxicity: Titanium dioxide is neither photo-irritant nor photo-allergenic to rabbits and guinea pigs respectively. It showed no evidence of sensitization in human volunteers. Photo genotoxicity assays have been conducted with the results showing that titanium dioxide is not photogenotoxic (SCCNFP, 2000). Human data: The working group of the International Agency for Research on Cancer (IARC) concluded that the epidemiological studies on titanium dioxide provide inadequate evidence of carcinogenicity (IARC Monograph, Volume 93, 2010). Others: Derived No Effect Level (DNEL) of 700 mg/kg bw/d for long term systemic exposure to titanium dioxide is given in the REACH Dossier. Dermal / percutaneous absorption: In vitro percutaneous absorption studies with coated or uncoated titanium dioxide indicate no dermal absorption. The in vitro absorption of microfine zinc oxide and titanium dioxide through porcine skin was reported in the REACH dossier (accessed on 05/03/2013 at http://echa.europa.eu). Titanium dioxide was not recovered in the receptor fluid; the potentially absorbable dose (total in the skin, stratum corneum and epidermis) was 0.1- 0.5%. Titanium dioxide applied in an oil/water emulsion base to the external surface of the arms showed deposition of the substance in the upper layer of the stratum corneum without any evidence of absorption reported. “Worst case” dermal absorption value of 0.5% is assumed. Margin of Safety (MoS): NOEL: 2500 mg/kg bw/d; Dermal absorption (Dap): 0.5%

Chemical Name: CI 77499

Function: Colour

Regulatory Status (Toxicological Risk Assessment Report):

Exposure	NOAEL	Safety Factors	MoS
ORAL	50 mg/kg bw/day	0	MoS For Adult: 30000.1

Summary Data:

Function: Approved colouring agents. Black Iron oxides. Chemically stable under normal conditions of use. Low level of use and the inert nature of iron oxides makes it unlikely for this substance to provoke an adverse effect. Iron oxide was practically nontoxic in male and female Wister rats LD50 > 5000mg/kg.bw. Inhalation of iron oxide fume (concentration 7 mg/m³ - mainly Fe2O3) did not produce any detectable effect in guinea pigs. It was not irritating to the skin or eyes of New Zealand white rabbits in OECD 404 and 405 studies respectively. It was not sensitizing to guinea pigs in the Maurer optimization test. No mutagenicity was observed in the chromosomal aberration test, gene mutation test and the Ames test. It has a low bioaccumulation potential based on study results . This substance is not carcinogenic or toxic to the reproductive system (ECHA, 2014) A NOAEL of 50 mg/kg bw/day can be concluded from an 8-generation reproductive toxicity study on rats (JECFA, 1980).

Chemical Name: CI 74160 (Pigment Blue 15)

Function: Colour

Regulatory Status (Toxicological Risk Assessment Report):

Exposure	NOAEL	Safety Factors	MoS
		0	MoS For Adult:

Summary Data:

A phthalocyanine pigment which is an approved colour in all cosmetic products. As supplied reported to lack potential to irritate the skin and minimally irritating to eyes. The acute oral LD50 is in excess of 10g/kg. If used at low concentrations unlikely to cause irritancy or sensitisation. Not based on aromatic amines. CI 74160 has been prohibited for use as a hair dye due to the bladder cancer risk (COMMISSION DIRECTIVE 2008/88/EC of 23 September 2008). Is included in Annex II to Directive 76/768/EEC. The United States shall adopt this provision from 14 Aug 2009.

Chemical Name: CI 77492 (Pigment Yellow Iron Oxide)

Function: Cosmetic Colorant - Colours cosmetics and/or imparts colour to the skin and/or its appendages.

Regulatory Status (Toxicological Risk Assessment Report):

Exposure	NOAEL	Safety Factors	MoS
ORAL	50 mg/kg bw/day	0	MoS For Adult: 300012

Summary Data:

Function: Approved colouring agent. Iron oxides are made of at least 60 % of iron and may not contain more than 1% of soluble matter. They are considered as inert ingredients, being almost insoluble in water but soluble in acids. Chemically stable under normal conditions of use. The insoluble colour pigment has low acute toxicity (oral LD50 >2000 mg/kg, rat). Non sensitising and

non irritating to the skin and eyes though it may cause mechanical eye irritation. Iron oxides and hydrated iron oxides were evaluated for an acceptable daily intake (ADI) for man (based on use as colours), by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and an ADI of 0.5 mg/kg bw was established. Iron oxides are naturally occurring mineral deposits and because they come from the earth may contain trace amounts of heavy metals. Iron oxides are used as colour pigments in a variety of applications; the ones use in cosmetic and personal care products are mainly synthetic and thus contain minute amounts of heavy metal as impurities. Iron oxides are regulated with regards to the levels of heavy metals that may be present in the raw material. Iron is an essential trace element required by all forms of life. In man it is required for the synthesis of haem proteins which function in the process of oxygen transport and oxidative metabolism. The haem proteins include haemoglobin, myoglobin, the cytochromes as well as catalase and peroxides. Iron occurs as a natural constituent of all foods of plant and animal origin, and may also be present in drinking water. In food it occurs in three forms - iron oxides, inorganic and organic salts, and organic complexes such as the haem iron. The total body iron for an adult male has been estimated to be about 4 g and for the female 2.5 g (ca. 38 mg/kg bw). The largest fraction of the iron is present in red cell haemoglobin, approximately 60% in the male and 85% in the female. The other major concentrations of iron occur in ferretin and haemosiderin, with lesser amounts in myoglobin, erythroid marrow and cell enzymes. Acute toxicity of iron ingested from normal dietary sources has not been reported. However, there are numerous reports of acute toxicity resulting from the ingestion of large overdoses of medicinal iron (particularly ferrous sulfate, a soluble form of iron), especially in small children. Iron overload which is very rare may cause increase in the body store of iron siderosis. There is no evidence that these deposits exert deleterious effects. However, severe cases of siderosis are associated with fibrosis and cirrhosis of the liver, as well as deposition of iron in the pancreas, adrenals, thyroid, pituitary and heart in a manner similar to that found in idiopathic haemochromatosis. The chemical form of iron is important in assessing its biological availability. Absorption of iron is regulated by the normal homeostatic process. Iron oxides and ferric hydroxide are virtually non-absorbable and therefore, unlikely to contribute significantly to body store of iron or causing siderosis. It is noted that in Ethiopia, contamination of cereal grain with iron-rich soil may result in an iron intake of approximately 500 mg/day. This has not been reported to cause siderosis because the contaminating iron is present in the form of iron oxide and hydroxides which are not readily available for absorption. Normally, individuals absorb less than 10% of dietary iron, or 1–2 mg per day balancing the daily loss from desquamation of epithelia (http://www.cdc.gov/ncbddd/hemochromatosis/training/pathophysiology/iron_cycle_popup.htm). No signs of toxicity was evident in a 8-generation reproduction study in rats continuously fed diet containing 570 mg of iron/lb as iron oxide (estimated daily dose was 25 mg of iron/kg bw/d. Also, in dogs that were fed from one to nine years on diets containing iron oxide colorant at 570 mg/lb; daily consumption was estimated at 428 mg/dog showed no significant effects. Assuming that JECFA applied a safety factor of 100 in deriving the ADI, the no observed adverse effect level (NO(A)EL) of 50 mg/kg bw/d is determined. Given that iron oxides are insoluble and non-absorbable, significant dermal penetration or uptake is not expected. As such, a dermal absorption value of 1% is applied as conservative estimate.

Chemical Name: CI 77491 (Iron Oxide red)

Function: Colour

Regulatory Status (Toxicological Risk Assessment Report):

Exposure	NOAEL	Safety Factors	MoS
ORAL	50 mg/kg bw/day	0	MoS For Adult: 30000.1

Summary Data:

Red Iron oxides, Essentially inert with minimal toxic properties (LD50 (rat, oral) >2000mg/kg). Non sensitizing and non irritating to the skin and eyes though it may cause mechanical eye irritation. Chemically stable under normal conditions of use. Low level of use and the inert nature of iron oxides makes it unlikely for this substance to provoke an adverse effect. However, JECFA has identified an ADI of 0-0.5 mg/kg bw (JECFA, 2008). REACH dossier: Inhalation and local DNEL 10 mg/m3 (10*10/70 = 1.42 mg/kg) (http://apps.echa.europa.eu/registered/data/dossiers/DISS-9eb9b2bd-9dfd-0981-e044-00144f67d031/AGGR-f8a66dce-55be-

43c3-a102-6c3513c58b3f_DISS-9eb9b2bd-9dfd-0981-e044-00144f67d031.html#AGGR-f8a66dce-55be-43c3-a102-6c3513c58b3f) The amount of dietary iron absorbed depends on many factors including dietary ingredients, source of dietary iron, iron content of the diet and the body needs for iron. Studies in which a single foodstuff biosynthetically labelled with Fe (vegetables grown in hydroponic media containing Fe, and meat from animals injected i.v. with Fe) was fed to normal human subjects showed that food iron of animal origin was better absorbed than that of vegetable origin (5-20% for meats, as opposed to 1-10% for vegetable iron). Maximum Oral absorption found in study data is 20%. INCI is water insoluble,so dermal absorption would be negligible (<10%). Dap 10% is considered conservatively. (http://www.inchem.org/documents/jecfa/jecmono/v18je18.htm) Iron Oxides are naturally occuring mineral deposits. These compounds are used as pigments in a variety of applications. Iron Oxides used in cosmetic and personal care products are synthetic. 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 the small amounts that may eventually be in cosmetic or personal care products do not pose a risk to human health. - See more at: http://www.cosmeticsinfo.org/ingredient/iron-oxides#sthash.G5oerWnT.dpuf Recommended daily allowance (RDA) for iron varies by age, gender, and, for females, whether they are pregnant or breastfeeding. For children ages four to eight years old, the RDA is 10 mg/day. For adults, the RDA ranges up to 27 mg/day for pregnant women. Upper limits representing levels that are likely to pose no adverse effects are 40 mg/day for children through 13 years old, and 45 mg/day for adults for iron. These upper limits correspond to 1.8 mg/kg/day for a 6-year-old 22.6-kg child, and 0.63 mg/kg/day for an average 71.8-kg adult (IOM 2002). Severe toxicity may result in children following ingestion of more than 0.5 g of iron. In adults, chronic excessive ingestion may lead to toxicity, manifested by hemosiderosis, disturbances in liver function, diabetes mellitus, and possible endocrine disturbances and cardiovascular effects (Amdur et al. 1991).
http://www.fs.fed.us/eng/aerial_ign/info/documents/riskasmt.pdf

Chemical Name: Mica (CI 77019)

Function: Opacifying (CosIng, 2013)

Regulatory Status (Toxicological Risk Assessment Report):

Exposure	NOAEL	Safety Factors	MoS
		0	MoS For Adult:

Summary Data:

Mica is silicate mineral with diverse chemical composition. Used in the production of pearlescent pigments and as a bulking agent in cosmetic products. The material is considered to be “chemically inert” and of a size unlikely to be inhaled (i.e. > 100 µm). There is low concern for systemic toxicity with non-respirable mica. It is not considered to be irritating to the skin or eyes and not known to cause skin sensitisation or elicitation of allergic reaction. Inhalation of mica dust over a period of years may cause fibrogenic response resulting in scarring of the lungs. Permitted for use in US, Canada and Saudi regulatory regimes.

High LD50 and not of toxicological concern (except for Mica that may contain crystalline quartz, which is known to be carcinogenic to humans [WHO, 2012; HSDB, 2012]. Because of the physico-chemical properties of mica, no cutaneous penetration is anticipated.

21CFR73.1496 - Mica may be safely used in amounts consistent with good manufacturing practice to color dentifrices and externally applied drugs, including those for use in the area of the eye.

21CFR73.2496 - Mica is safe for use in coloring cosmetics generally, including cosmetics applied to the area of the eye, in amounts

consistent with good manufacturing practice.

21CFR176.170 - INDIRECT FOOD ADDITIVES: PAPER AND PAPERBOARD COMPONENTS.

21CFR177.2600 - INDIRECT FOOD ADDITIVES: POLYMERS, Rubber articles intended for repeated use

21CFR178.3297 - INDIRECT FOOD ADDITIVES: ADJUVANTS, PRODUCTION AIDS, AND SANITIZERS, Colorants for polymers.

Margin of Safety Calculation

INCI Name	Conc. (% w/w)	SED mg/kg	NOAEL/NOEL mg/kg bw/day	MoS
ACRYLATES COPOLYMER	70	0.14000000	250	1785.7
HEMA	20	0.16700000	30	180
BUMETRIZOLE	5	0.04200000		
CI 77891	3	0.00000000	2500	19998400.1
CI 77499	2	0.00200000	50	30000.1
CI 74160	2	0.01700000		
CI 77492	2	0.00000000	50	300012
CI 77491	2	0.00200000	50	30000.1
MICA	2	0.00000000		

Note: In the absence of NO(A)EL data, the Margin of Safety (MoS) has not been calculated.
Unless otherwise determined and in the absence of literature or other experimental data, a Dermal Absorption (DAp) of 100% is taken as the worst case scenario.
NO(A)EL: No Observed Adverse Effect Level; MoS: Margin of Safety; SED Systemic Exposure Dosage
Calculation of Margin of Safety: MoS = NO(A)EL / SED

References for skin surface area, exposures, body weight and application quantities are derived from EU guidance and literature sources.
These are held on file at intertek.

The following conditions apply to this assessment:
1. This product was not evaluated for heavy metal or lead content by the undersigned.
2. This product was not assessed for compliance with regulations, other than as described above, by the undersigned.
3. This product has not been evaluated for potential physical injury such as choking hazard, aspiration risk, or mechanical irritation by the undersigned.
4. It was assumed that all ingredients in the product were disclosed and are accurate as listed in the report table, subject to valid request.
5. Based upon the information supplied, unless otherwise stated in this report and subject to a valid request, being made, it was assumed that neither this product, nor the ingredients used in the product, contained any impurities/contaminants that would cause toxicity in a consumer.
6. This evaluation is relevant solely to the conditions described herein. Any substitution of ingredients, increase in concentrations of use, or change of use pattern will necessitate a new evaluation.
"Valid request" refers to request from supplier of formulation to Intertek.
7. Toxicological profiles are stored within an in-house database at Intertek.

For European Legislation only: This formulation will be assessed by Intertek in accordance with PART B , Annex I to Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products (Official Journal L 342, 22 December 2009, pp. 59–209). The safety assessment is based upon the chemical specification and toxicological profile of the ingredients as supplied at the time of assessment and an assessment of the final cosmetic product. The supplier to this safety assessment is advised to ask for a new safety evaluation if any change in formulation occurs, change in raw materials used, abnormally high number of adverse events are recorded, changes in recommended uses or other circumstances that may affect the safety of this product.

END OF REPORT

This report is made solely on the basis of your instructions and/or information and materials supplied by you. It is not intended to be a recommendation for any particular course of action. Intertek does not accept a duty of care or any other responsibility to any person other than the Client in respect of this report and only accepts liability to the Client insofar as is expressly contained in the terms and conditions governing Intertek's provision of services to you. Intertek makes no warranties or representations either express or implied with respect to this report save as provided for in those terms and conditions. We have aimed to conduct the Review on a diligent and careful basis and we do not accept any liability to you for any loss arising out of or in connection with this report, in contract, tort, by statute or otherwise, except in the event of our gross negligence or wilful misconduct.