Safety Assessment of Vinylpyrrolidone Polymers as Used in Cosmetics

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All interested persons are provided 60 days from the above date to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Executive Director, Dr. Bart Heldreth.

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INTRODUCTION

The safety of the following 30 ingredients, as used in cosmetics, is being reviewed in this safety assessment:

VP/Hexadecene Copolymer
VP/Eicosene Copolymer
Acrylates/Stearyl Methacrylate/VP Copolymer
Acrylic Acid/VP Crosspolymer
Butylated PVP
Ethylhexyl Acrylate/VP/Dimethicone Methacrylate Copolymer
Ethylhexyl Methacrylate/Methyl Methacrylate/VP Copolymer
Hydrolyzed Wheat Protein/PVP Crosspolymer
Maltodextrin/VP Copolymer
PVP/Decene Copolymer
PVP/VA/Itaconic Acid Copolymer
PVP/VA/Vinyl Propionate Copolymer
Triacontanyl PVP
Triacontene/VP Copolymer
Vinyl Caprolactam/VP/Dimethylaminoethyl Methacrylate Copolymer
VP/Acrylates/Lauryl Methacrylate Copolymer
VP/Dimethiconylacrylate/Polycarbamyl/Polyglycol Ester
VP/Dimethylaminoethylmethacrylate/Polycarbamyl Polyglycol Ester
VP/DMAPA Acrylates Copolymer
VP/Polycarbamyl Polyglycol Ester
VP/Vinyl Alcohol Copolymer
VP/Vinyl Caprolactam/DMAPA Acrylates Copolymer
Acrylates/VP Copolymer**
Ammonium Acryloyldimethyltaurate/VP Copolymer*
Methacrylic Acid/Styrene/VP Copolymer*
PVP*
Sodium Acryloyldimethyltaurate/VP Crosspolymer*
Styrene/VP Copolymer*
VP/Dimethylaminoethylmethacrylate Copolymer**
VP/VA Copolymer*

*Previously reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel (Panel)
**Previously reviewed by the Panel, and a rereview of this safety assessment is ongoing

Most of these ingredients have the film former function in cosmetics in common (see Table 1).[1] Viscosity increasing agent and binder are two other functions that are frequently being reported.

It should be noted that the Panel has evaluated the safety of and issued conclusions (in published reports) on 8 ingredients/ingredient groups (identified with an asterisk above) that are similar to the 22 ingredients that are being reviewed for the first time in this safety assessment. The Panel's published conclusions on the 8 ingredients/ingredient groups previously reviewed are stated in Table 2, and the published reports may be found at https://www.cir-safety.org/ingredients. Data on other polymers that were reviewed in these published safety assessments that may have been used to evaluate safety in the absence of data on the polymers that were being evaluated are not included in this safety assessment. The published reports may be consulted for safety test data on those polymers, as well as the available data on monomers. Safety test data on vinylpyrrolidone polymers (i.e., polymers that are the subject of this review) that are included or referenced in the published reports (italicized within the text of this safety assessment) and ingredient use frequency/use concentration data (both current data and data from a published CIR report) are included in this safety assessment. Data on vinylpyrrolidone polymers that were published since the most recent published CIR safety assessment on any of these ingredients are also included. Information relating to the CIR review status of the monomer components of vinylpyrrolidone polymers is presented in Table 3.

This safety assessment includes relevant published and unpublished data for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A list of the typical search engines and websites used, sources explored, and endpoints that CIR evaluates, is available on the CIR website (http://www.cir-

safety.org/supplementaldoc/preliminary-search-engines-and-websites; http://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

CHEMISTRY

Definition and General Characterization

The definitions, structures, and functions of the vinylpyrrolidone copolymers that are reviewed in this safety assessment are presented in Table 1. These polymeric ingredients share in common a vinylpyrrolidone monomer (Figure 1).

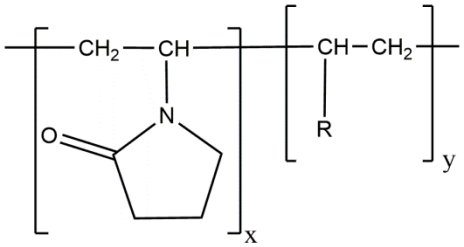


Figure 1 Polyvinylpyrrolidone ingredients (wherein –C(R)HCH$_2$- represents at least one co-monomer residue).

Chemical and Physical Properties

The physical properties of 5 vinylpyrrolidone polymers are presented in Table 4. Maltodextrin/VP Copolymer has an average molecular weight of 132,999 Da.[2] Triacontanyl PVP (as a trade name material), another high molecular weight polymer, is insoluble in water, acid, or base solution.[3] VP/Acrylates/Lauryl Methacrylate Copolymer is expected to have low water solubility based on its mostly hydrophobic structure.[4] Sodium Acryloyldimethyltaurate/VP Crosspolymer is miscible with water and VP/Dimethylaminoethylmethacrylate Copolymer has a density of 1.047 g/cm^3.[5,6] Additionally, the molecular weight of PVP can range from 10,000 to 700,000 Da, and PVP K-25 and K-30 (average molecular weight = 40,000 Da) are commonly used in cosmetic formulations.[7]

VP/VA Copolymer

VP/VA Copolymer does not absorb energy over the UVA, UVB, or visible light spectrum.[8]

Method of Manufacture

VP/VA Copolymer

VP/VA Copolymer is prepared by free radical polymerization in ethyl alcohol.[8]

VP/VA copolymer is produced by free radical copolymerization of N-vinyl-2-pyrrolidone (NVP) and vinyl acetate (VA) in solution in isopropanol, in the presence of initiators.[9] The process is continuous and temperature controlled. Hydrazine is formed from amines present in this reaction mixture. Sodium bisulfite is added to the batch for color stability. Isopropanol is exchanged for deionized water by adding deionized water to the reactor and performing a solvent exchange via vacuum distillation. Sodium acetate (for pH stabilization) and a microbiological preservative (not specified) are added. The batch is then heated, sampled, and adjusted for solids content. The product is isolated as an aqueous solution, or as a spray-dried solid.

Composition/Impurities

Acrylates/VP Copolymer and VP/Dimethylaminoethylmethacrylate Copolymer

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.[10]

Ammonium Acryloyldimethyltaurate/VP Copolymer and Sodium Acryloyldimethyltaurate/VP Crosspolymer

Ammonium Acryloyldimethyltaurate/Carboxyethyl Acrylate Crosspolymer was reported to be >90% pure. Sodium Polyacryloyldimethyl Taurate is reported to contain <2000 ppm AMPS and <10 ppm acrylamide.[11]

Australia's National Industrial Chemical Notification and Assessment Scheme (NICNAS) has noted that Sodium Acryloyldimethyltaurate/VP Crosspolymer contains residual monomers and/or impurities (not stated) that are classified as hazardous according to the *Globally Harmonized System of Classification and Labeling of Chemicals (GHS)*, as adopted for industrial chemicals in Australia.[5]

Maltodextrin/VP Copolymer

Maltodextrin/VP Copolymer, a high molecular weight polymer (132,999 Da), contains an unnamed low molecular weight species that is <1000 Da (0.8% of composition) and an unnamed low molecular weight species that is < 500 Da (0.1% of composition). [2]

Methacrylic Acid/Styrene/VP Copolymer

Data provided by industry indicate that styrene and vinyl-type styrene copolymer trade name materials contain styrene monomer at levels of < 100 ppm or less.[12]

PVP

The USP specifies that pharmaceutical grade PVP cannot contain more than 1 ppm hydrazine.[7]

PVP, an NVP-containing polymer, is imported into Australia for industrial uses, and the residual NVP monomer levels in PVP were obtained from a few (number not stated) major importers of PVP.[13] It was noted that it appears that there are different grades of PVP imported into Australia, depending on the end use (i.e., pharmaceutical, cosmetic, or industrial grade). The residual NVP monomer content in the PVP imported into Australia varies and ranges from 10 ppm to 2000 ppm. In Europe, NVP residues in PVP are generally below 100 ppm.

Triacontanyl PVP

According to one source, Triacontanyl PVP has a purity of > 97% and consists of < 2% water.[3]

VP/VA Copolymer

VP/VA Copolymer is supplied either in 100% concentration as a powder or as a 50% solution in alcohol.[8] *VP/VA Copolymers may contain the residual monomers, vinyl acetate at 1.0%, and vinyl pyrrolidone at 0.5%.*

For VP/VA copolymers with molecular weights of approximately 12,000 and greater, the level of vinyl acetate is smaller than or equal to 300 ppm as measured using HPLC.[14] *Another source reported vinyl acetate levels of less than 100 ppm for copolymers of molecular weights of 12,700 to approximately 30,000, and levels of less than 1000 ppm for a copolymer of a molecular weight of approximately 51,000.*

Specifications for VP/VA Copolymer that were submitted to the European Food Safety Authority (EFSA) are presented in Table 5. Some of the specifications relate to monomer content and impurities.[9]

USE

Cosmetic

The safety of vinylpyrrolidone polymers is evaluated based on data received from the U.S. Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in FDA's Voluntary Cosmetic Registration Program (VCRP) database.[15] Use concentration data are submitted by the cosmetics industry in response to surveys, conducted by the Council, of maximum reported use concentrations by product.[16]

According to 2018 VCRP data, the greatest use frequency is being reported for PVP, which is being used in 900 cosmetic products (798 leave-on products + 101 rinse-off products + 1 product diluted for bath use).[15] The second highest use frequency (597 cosmetic products: 525 leave-on products + 62 rinse-off products) is being reported for Ammonium Acryloyldimethyltaurate/VP Copolymer. In general, the differences in current use frequencies of vinylpyrrolidone polymers in cosmetics versus those reported in previous years are unremarkable. The results of a concentration of use survey conducted in 2017 indicate that VP/VA Copolymer is being used at concentrations up to 44% in rinse-off products (paste masks and mud packs), which is the highest maximum ingredient use concentration that is being reported for vinylpyrrolidone polymers.[16] Notably, in 2003, the highest maximum use concentration of VP/VA Copolymer in rinse-off products was 10%, which is 4-fold lower than the current highest maximum use concentration in rinse-off products.[14] The highest maximum ingredient use concentration of vinylpyrrolidone polymers in leave-on products is being reported for PVP, which is being used at concentrations up to 35% in leg and body paints. Notably, in 2013, the highest maximum use concentration of PVP in leave-on products was lower, 12%. Thus, the highest maximum use concentration of PVP in leave-on products is approximately 3-fold greater than the highest maximum use concentration of this ingredient in leave-on products that was reported in 2013. Current and historical use frequency and concentration of use data are presented in Table 6.

According to VCRP and Council survey data, the following 9 vinylpyrrolidone polymers are not being used in cosmetic products:

Acrylates/Stearyl Methacrylate/VP Copolymer
Ethylhexyl Acrylate/VP/Dimethicone Methacrylate Copolymer
Ethylhexyl Methacrylate/Methyl Methacrylate/VP Copolymer
Methacrylic Acid/Styrene/VP Copolymer
PVP/Decene Copolymer
PVP/VA/Itaconic Acid Copolymer
PVP/VA/Vinyl Propionate Copolymer
Triacontene/VP Copolymer
VP/Vinyl Alcohol Copolymer

Cosmetic products containing vinylpyrrolidone polymers may be applied to the skin and hair or, incidentally, may come in contact with the eyes (e.g., at maximum use concentrations up to 17.2% VP/Hexadecene Copolymer [in eye shadows]) and mucous membranes (e.g., at maximum use concentrations up to 24.1% VP/Hexadecene Copolymer [in lipstick]). The incidental ingestion of ingredients may result from the use of lipstick products. Products containing vinylpyrrolidone polymers may be applied as frequently as several times per day and may come in contact with the skin or hair for variable periods following application. Daily or occasional use may extend over many years.

VP/VA Copolymer is being used in both pump hair sprays (maximum use concentrations up to 9%) and aerosol hair sprays (maximum use concentrations up to 10%), which may result in incidental inhalation exposure. These 2 concentrations are the highest maximum cosmetic use concentrations that are being reported for vinylpyrrolidone polymers in cosmetic products that are sprayed In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 μm, with propellant sprays yielding a greater fraction of droplets/particles below 10 μm, compared with pump sprays.[17,18,19,20] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[17,18]

VP/Eicosene Copolymer is being used in face powders at concentrations up to 0.5% (highest maximum use concentration). Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[21,22,23]

The ingredients reviewed in this safety assessment do not appear on the list of substances that are prohibited in cosmetic products that are marketed within the European Union and are not subject to any restrictions relating to their use in these products.[24]

Noncosmetic

PVP

PVP is cleared for the following uses: as a clarifying agent in beverages and vinegar; as a tableting adjuvant; and as a stabilizer, bodying agent, and dispersant in nonnutritive sweeteners in concentrated liquid form, and vitamin and

mineral concentrates. It is also cleared for use in packaging that comes in contact with various foods. PVP K-30 (average MW 40,000) is used as a food additive.

PVP is used widely in industries such as pharmaceuticals, adhesives, agriculture, and surface coating.[13] It is used in medicine and in the pharmaceutical industry as a blood plasma expander, and it is a common ingredient in drug manufacture.[25]

VP/VA Copolymer

The EFSA Panel on Food Additives and Nutrient Sources added to Food has provided a scientific opinion on the use of VP/VA Copolymer in food supplements.[9] This opinion addresses the safety of VP/VA Copolymer for use in food supplements, in tablet form as a binding/coating agent in an amount of up to 10% of weight per tablet, for a tablet weight of 1000 mg. Overall, the Panel concluded that the use of VP/VA copolymer in solid food supplements as a binding/coating agent is unlikely to be a safety concern at the proposed uses and use levels provided. The Panel also concluded that the residual level of hydrazine, proposed at a maximum of 1.0 mg/kg in the final product, is unlikely to be of safety concern. However, the Panel noted that it would be prudent to lower the level of hydrazine as far as reasonably achievable.

TOXICOKINETIC STUDIES

Absorption, Distribution, Metabolism, and Excretion

Animal

Oral

PVP

The absorption, distribution, metabolism, and excretion of PVP is dependent on molecular weight, amount and frequency of dosing, and route of administration.[7] Polymers with a weight < 25,000 are eliminated through the kidneys. An oral dosing study using 0.9 mg per rat of a PVP trade name material found no significant absorption.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Animal

Dermal

Triacontanyl PVP

A single dose of a Triacontanyl PVP trade name material (moistened with water, dose = 2 g/kg) was applied, under an occlusive wrap, for 24 h to the backs of 10 New Zealand white rabbits.[3] The animals were observed for up to 14 days after test substance application, and all gained weight during the study. None of the animals died, and no abnormal clinical signs were observed. The acute dermal LD_{50} was > 2 g/kg.

Oral

Ammonium Acryloyldimethyltaurate/VP Copolymer

The acute oral LD_{50} for Ammonium Acryloyldimethyltaurate/VP Copolymer was reported to be >2000 mg/kg in rats.[11]

PVP

The oral LD_{50} of PVP (avg. MW of 40,000) is > 100 g/kg body weight for both rats and guinea pigs.[7]

Triacontanyl PVP

The acute oral toxicity of a Triacontanyl PVP trade name material was evaluated using 10 Sprague-Dawley rats (5 males, 5 females).[3] A single 5 g/kg oral dose of the test substance (ground into a powder and mixed with peanut butter and honey) was fed to the animals. The test substance was consumed within 18 h to 24 h. Dosing was followed by a 14-day observation period. None of the animals died and no gross organ changes were observed at necropsy. The LD_{50} was > 5 g/kg.

VP/Acrylates/Lauryl Methacrylate Copolymer

An LD_{50} of > 5 g/kg (rats) has been reported for undiluted VP/Acrylates/Lauryl Methacrylate Copolymer.[4] Dyspnea was observed in 1 animal. The number of animals tested and details relating to the test protocol and study results were not specified.

VP/VA Copolymer

Acute oral toxicity studies were performed with VP/VA Copolymer in formulation and in solutions of the raw ingredient. Tests on mice and rats showed low to no toxicity on more than 76 animals. Two animals died from administration of a formulation containing other, unidentified ingredients. The surviving animals showed, at most, decreased activity and ataxia at maximum doses of 5 g/kg of a solution containing 12.5% VP/VA Copolymer.[8]

Short-Term Toxicity Studies

Dermal

VP/VA Copolymer

A hair product containing 1% VP/VA Copolymer was tested in a six-week dermal toxicity study on 50 albino rats. Volumes of 2.0 ml/kg of the product were applied five days a week for six weeks for a total of 30 applications to the clipped skin of the animals. All rats survived, and their body weight, physical appearance, behavior, and gross and microscopic anatomy were normal. No systemic toxic effects could be attributed to the test material.[8]

Oral

VP/VA Copolymer

VP/VA Copolymer was administered in the diet of 3 groups of male and female Sprague-Dawley rats (5 animals/sex/group; control group: 5 animals/sex) for 28 days at doses of 0 (control), 100, 300, and 1000 mg/kg/day, respectively.[9] The control group was fed the basal diet only. All animals survived to the scheduled necropsy. There were no clinical signs of toxicity, and there were no effects on the following: body weight gain, feed consumption, hematology parameters, serum chemistry, and urinalyses. There also were no test substance-related effects on organ weights, macroscopic and microscopic evaluations. The authors concluded that the no-observed-adverse-effect level (NOAEL) was 1000 mg/kg/day.

PVP

In two short-term inhalation studies using rats, PVP was detected in lung samples but no inflammatory response was noted. Mild lymphoid hyperplasia and fibroplasia were noted in the subpleural, perivascular, and peribronchial lymphatics.[7]

The short-term oral toxicity of a PVP tradename material (5% w/v in water) was evaluated using 2 groups of 6 HanWistar rats (RccHan:WIST; 3 males, 3 females/group).[26] The test animals received oral doses (dose volume of 10 ml/kg, by gavage) daily for 28 consecutive days. The control group received water. At day 1 after the final dose, the animals were killed and scheduled for necropsy. The following tissues were examined microscopically: eyes, liver, kidneys, urinary bladder, lungs, heart, thymus, sternum, upper jaw (with nares and nasal turbinates), lower jaw with skin, stomach/duodenum, intestine (jejunum, ileum, cecum, and rectum), mesenteric lymph node, and the tongue. All hematology findings were within the normal background range for the rat strain that was tested, and there was no induction of cytochrome P450 protein (CYP1A1/2, CYP2B1, CYP3A, and CYP4A) levels. There were no toxicologically relevant effects on body weight gain, food consumption, or water consumption, and there were no treatment-related microscopic changes.

Subchronic Toxicity Studies

Oral

VP/VA Copolymer

VP/VA Copolymer was administered in the diet of 3 groups of male and female Sprague-Dawley rats (10 animals/sex/group; control group 10 animals/sex) for 90 days at doses of 0 (control), 100, 300, and 1000 mg/kg/day, respectively.[9] The control group was fed the basal diet only. All animals survived to the scheduled necropsy. There were no clinical signs of toxicity, and there were no effects on the following: body weight gain, feed consumption, functional observational battery, and locomotor activity evaluations. Furthermore, there were no ophthalmic lesions indicative of toxicity, and no test-substance-related effects on hematology parameters, serum chemistries, and urinalyses. No test substance-related effects on organ weights, macroscopic, and microscopic evaluations were observed. The authors concluded that the NOAEL was 1000 mg/kg/day.

Inhalation

VP/VA Copolymer

Rats and hamsters were exposed for 13 weeks to a spray containing 4.0% VP/VA Copolymer.[8] *Each of three groups comprised of 12 rats and 12 hamsters per group inhaled the spray for four hours per day, five days per week for 13 weeks in doses of 5.4 mg/m3 (calculated to be the equivalent of one hundred times the normal human use level of the product). No gross or microscopic changes occurred that could be attributed to the test material. Lungs and other tissues were similar in control and tested animals. Subchronic inhalation of a spray formulation containing 1.72% VP/VA Copolymer for 90 days produced no effects in rabbits.*

Chronic Toxicity Studies

Animal

Oral

PVP

Neither toxic effects nor gross lesions attributable to PVP were found in rats maintained for 2 years on a diet containing up to 10% of a PVP trade name material. A similar 2-year feeding study in dogs found swollen phagocytic cells in the lymph nodes.[7]

VP/VA Copolymer

Chronic (1 year) oral ingestion of a solution containing 10.2 mg/l of VP/VA Copolymer produced no effects in mice or rats.[8]

In a 52-week oral feeding (diet) study, the chronic oral toxicity of VP/VA Copolymer was evaluated using the following groups of male and female pure-bred beagle dogs: group 1 (4 males, 4 females: 510 mg/kg/day), group 2 (4 males, 4 females: 1518 mg/kg/day), and group 3 (6 males, 6 females: 2522 mg/kg/day).[27] The control group was fed a diet without the test substance. All animals were killed at the end of the dosing period, and both gross and histopathologic examinations were performed. None of the animals died during the study and no treatment-related clinical signs were observed. Furthermore, the following parameters were unaffected by treatment: food consumption, ophthalmoscopic examinations, hearing tests, electrocardiograms, and blood pressure. There were no treatment-related body weight losses during the study. Hematology, clinical biochemistry, and urinalysis parameters were unaffected by feeding with the test substance; sporadic statistically significant intergroup differences were observed, but these findings were not dose-related. Therefore, differences in these parameters were considered to represent the expected spontaneous variations that occur in dogs of the age and strain that are being used in this study.

There were no treatment-related or dose-related changes in organ weights or organ-to-body weight ratios. At gross examination, the type and incidence of findings were comparable between test and control groups. At microscopic examination, the incidence and severity of findings were comparable between test and control groups and were considered commonly observed changes in dogs of the age and strain used in this study. No inflammatory and/or degenerative changes (i.e., necrosis, granulomas, etc.) were associated with vacuolated histiocytes that were diagnosed in the sinusoids and

trabeculae of some mesenteric lymph nodes. The NOAEL was determined to be the target dose of 2500 mg/kg/day (target dose for highest dose group).[27]

The chronic oral toxicity of VP/VA Copolymer was evaluated using 3 groups of male and female Wistar rats of the Chbb:THOM (SPF) strain (50 males, 50 females/group).[27] The 3 groups were fed the test substance (in the diet) at the following doses for 24 months: group 1 (high dose: 686 mg/kg/day [males] and 691 mg/kg/day [females]), group 2 (mid dose: 1374 mg/kg/day [males] and 1378 mg/kg/day [females), and group 3 (low dose: 2625 mg/kg/day [males] and 2759 mg/kg/day [females]). A fourth group (control) was fed a diet without the test substance for the same duration. The test substance (same doses) was also fed to 4 satellite groups (4 test and 1 control) for 18 months. These 4 groups were included for hematological evaluation. For all groups in the study, the animals were killed after a 16-h to 20-h fasting period that began after the end of the dosing period. Numerous tissues were submitted for histopathological examination. The mortality rates ranged from 14% in the high-dose males to 36% in the control males, and 26% in the high-dose females to 30% in the control females. Data were comparable in the satellite groups. Food consumption was described as normal. Due to the absence of a dose-response relationship, and a higher mortality rate in control rats of both sexes, it was concluded that the test substance did not affect survival. No remarkable test substance-related clinical signs were observed in the study. Body weight and body weight change were statistically significantly reduced in high-dose males at most time points throughout most of the study. Marginal differences in hematological parameters (within historical control ranges) were observed, but there was no dose-response relationship and the differences were not considered treatment-related. The vast majority of the gross lesions in the main groups in the study were comparable to the incidence in controls, and there was no clear dose-response relationship. The NOAEL was determined to be the target dose of 2800 mg/kg/day (target dose for highest dose group). Results relating to tumor formation are included in the Carcinogenicity section of this report.

A 2-year feeding study on VP/VA Copolymer (60% VP and 40% VA) was performed using 2 groups of Sprague-Dawley rats (51 males and 51 females/group, test and control groups).[9] Test animals were given feed containing 5% VP/VA Copolymer, and control animals were given feed containing 5% cellulose. Based on the consumption of the entire diet, test animals were fed ~0.67 g VP/VA Copolymer (equivalent to ~450 mg/kg/day) for the duration of the study. Hemoglobin content and leukocyte count were determined in 5 rats per sex (test and control groups) for up to 364 days of the study. Hematology, blood chemistry, and urinalysis parameters were evaluated after ~500 days of the study. These 3 parameters were evaluated using 10 test and control rats of each sex, as well as in all test (20 rats) and control (11 rats) animals that remained alive after 675 days. Survival in both the control and test groups was described as poor (8% to 14%), due to inflammatory diseases of the respiratory tract. There were no signs of toxicity in test or control rats, and no treatment-related clinical chemistry changes. At histopathological examination of organs (liver, kidneys, and other organs [not stated]), an increased incidence of liver congestion and fatty degeneration in the test group, compared to the control group, was reported. No gross pathologically detectable lesions were observed. Results relating to carcinogenic potential are included in the Carcinogenicity section of this report.

Inhalation

VP/VA Copolymer

Chronic (2 years) inhalation exposure to hair spray aerosols containing 0.08 ± 0.08 mg/l and 0.35 ± 0.09 mg/l for 2 years produced no effects in hamsters.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

In Vitro

PVP

No teratogenic effects were observed when up to 500 µg of PVP (MW 11,500) was injected into the yolk sac of rabbit embryos.[7]

GENOTOXICITY STUDIES

In Vitro

Ammonium Acryloyldimethyltaurate/VP Copolymer

Ammonium Acryloyldimethyltaurate/VP Copolymer was not mutagenic in bacterial reverse mutation assays.[11]

PVP

PVP was negative in the majority of mutagenicity studies conducted.[7] *The in vitro assays that were performed in these studies included Ames, mouse lymphoma, and Balb/c 3T3 tests.*

Three formulations containing PVP-iodine were not genotoxic in a comet assay or a chromosome aberration test, with or without metabolic activation.[28] *The solutions contained 3% or 10% PVP-iodine. In both tests, CHO-K1 cells were exposed for 4 h to the test solutions. Expected results were observed with positive and negative controls.*

The genotoxicity of PVP was evaluated in the Ames test using the following *Salmonella typhimurium* strains: TA98, TA100, TA1535, and TA1537.[29,30] Each strain was tested with 10% PVP (in water) with and without metabolic activation. The results were classified as negative in all bacterial strains, with and without metabolic activation.

Sodium Acryloyldimethyltaurate/VP Crosspolymer

The genotoxicity of Sodium Acryloyldimethyltaurate/VP Crosspolymer was evaluated in the Ames test (bacterial strains and doses not stated) (Organization for Economic Co-operation and Development (OECD) Test Guideline (TG) 471).[5] The test substance was classified as non-genotoxic.

Triacontanyl PVP

The genotoxicity of a Triacontanyl PVP trade name material was evaluated in the Ames test using the following *Salmonella typhimurium* strains: TA98, TA100, TA1535, TA1537, and TA1538.[3] The test substance was evaluated (with and without metabolic activation) at doses up to 2500 µg/plate. 2-Aminoanthracene, 2-nitrofluorene, sodium azide, and ICR-191 served as positive controls. The test substance was not genotoxic in any of the *Salmonella typhimurium* strains tested. Marked increases in the number of revertant colonies were observed in positive control cultures.

In Vivo

PVP

PVP was negative in the majority of the in vivo mutagenicity studies conducted.[7] *The assays that were performed were dominat lethal, micronucleus, and Chinese hamster bone marrow tests.*

CARCINOGENICITY STUDIES

Animal

Oral

VP/VA Copolymer

The carcinogenicity of VP/VA Copolymer was evaluated using 3 groups of male and female Wistar rats of the Chbb:THOM (SPF) strain (50 males, 50 females/group).[27] The 3 groups were fed the test substance (in the diet) at the following doses for 24 months: group 1 (low dose: 2625 mg/kg/day [males] and 2759 mg/kg/day [females]), group 2 (mid dose: 1374 mg/kg/day [males] and 1378 mg/kg/day [females), and group 3 (high dose: 686 mg/kg/day [males] and 691 mg/kg/day [females]). A fourth group (control) was fed a diet without the test substance for the same duration. At histopathological examination, there was no treatment-related increase in the number of animals with the following: neoplasms (primary neoplasm or benign, malignant, systemic and metastasized neoplasms). There also was no treatment-related increase in the total number of primary neoplasms, or benign, malignant, systemic, or metastasized neoplasms. Additionally, there was no indication that the test substance caused any non-neoplastic alteration of organs or organ systems, when comparing the incidence and graded severity of microscopic findings of treated animals with the corresponding observations in control animals. All neoplastic and non-neoplastic microscopic findings were considered to have developed spontaneously and were not related to treatment.

A 24-month feeding study on VP/VA Copolymer (60% VP and 40% VA) was performed using 2 groups of Sprague-Dawley rats (51 males and 51 females/group, test and control groups).[9] Test animals were given feed containing 5% VP/VA Copolymer, and control animals were given feed containing 5% cellulose. Based on the consumption of the entire

diet, test animals were fed ~0.67 g VP/VA Copolymer (equivalent to ~450 mg/kg/day) for the duration of the study. No treatment-related tumors or other gross pathologically detectable lesions were induced.

Implantation

PVP

Implantation of PVP sponges into mice and rats resulted in development of local sarcomas, but without metastases.[7]

ANTICARCINOGENICITY STUDY

PVP

Orally administered PVP significantly decreased the rate of bladder tumors in mice exposed to bracken fern. IARC classified PVP as a "group 3" agent, "not classifiable as to its carcinogenicity in humans."[7]

OTHER RELEVANT STUDIES

Cytotoxicity

PVP

A study was performed to evaluate the effects of PVP amphiphilic polymers and polymeric nanoparticles on MCF-7 cell (human cancer cell line) growth and viability, using the MTT (thiazoyl blue tetrazolium bromide) cell viability assay.[31] The PVP amphiphilic polymers that were used to prepare the nanoparticles were defined as follows: PVP-OD4000 (amphiphilic N-vinylpyrrolidone polymer with molecular weight of hydrophilic polymer fragment of 4000 Da and 1 hydrophobic octadecyl group), PVP-OD8000 (amphiphilic N-vinylpyrrolidone polymer with molecular weight of hydrophilic polymer fragment of 8000 Da and 1 hydrophobic octadecyl group), and PVP-$DD_2$4000 (amphiphilic N-vinylpyrrolidone polymer with molecular weight of hydrophilic polymer fragment of 4000 Da and 1 hydrophobic di(dodecyl) group). Amphiphilic PVP polymeric nanoparticles were prepared using an emulsification and solvent evaporation technique. The particle sizes of the PVP-OD4000, PVPOD8000, and PVP-$DD_2$4000 nano-aggregates were 32 nm, 47 nm, and 86 nm, respectively. MCF-7 cells were incubated with each type of unassociated polymer (PVP-OD4000, PVP-OD8000 and PVP-DD24000) or nanoparticles for 24, 48 or 72 h before MTT assays were performed. Polymer concentrations ranged from 0.05% to 0.5%, and nanoparticle concentrations ranged from 0.5% to 5%. Additionally, the critical aggregation concentration (CAC) of amphiphilic PVP polymers was determined using pyrene fluorescence probe spectrometry. The CACs of all 3 polymers were in the micromolar range (6.2 to 14.6 µm/l).

Polymers with an n-alkyl octadecyl hydrophobic group demonstrated low cytotoxic effects against MCF-7 cells (compared to untreated control cells) ($P < 0.05$). PVP$DD_2$4000 nanoparticles were slightly more cytotoxic due to the presence of more branched hydrophobic groups. All polymers demonstrated no cytotoxicity both at concentrations less than the critical aggregation concentration (simple polymer solution) and at higher concentrations, when amphiphilic macromolecules are self-assembled in nanoparticles ($P < 0.05$). For example, incubation with PVP-OD4000 and PVP-OD8000 at concentrations as high as 5% resulted in cell viabilities of 99%. Furthermore, the corresponding nanoparticles did not cause marked cell death ($P < 0.05$).[31]

The effect of PVP on the ultrastructure of spermatozoa from 12 fertile patients was evaluated.[32] A sperm suspension (0.1 ml) from each patient was added to a 10% PVP solution (0.5 ml) and incubated for 30 minutes. An aliquot of the sperm suspension without PVP served as the control. The samples were analyzed by transmission electron microscopy. Results indicated that the untreated sperm fractions and the PVP-treated fractions were significantly different. The means of the percentages of spermatozoa devoid of defects in untreated sperm fractions versus PVP-treated fractions were 4.2808% and 0.5490%, respectively ($P = 0.001$). The sperm organelles that were deteriorated by PVP treatment were as follows: swollen, reacted or absent acrosomes, the granular and decondensed chromatin, and swollen and badly shaped mitochondria. The most affected organelle was the plasma membrane, which appeared broken in a high percentage of the cells. In cross sections of sperm tails after PVP treatment, the plasma membrane was broken, the mitochondria were swollen, and the axoneme was disassembled. Thus, PVP strongly affected the fine structure of spermatozoa. The authors concluded that PVP exerted a disintegrating effect on the various kinds of sperm membranes, and, as a secondary consequence of the eventual necrotic process, alteration of chromatin and cytoskeletal components.

The effect of a PVP tradename material on cultured HeLa cells (human cervical carcinoma cells) was evaluated.[33] He La cells were incubated for 24 h at concentrations of 5%, 10%, and 20%. Treatment with the test substance produced a dose- and time-dependent toxicity (i.e., inhibitory effect on cell proliferation) to HeLa cells. The hallmarks of apoptosis, such as chromatin condensation, DNA fragmentation, and formation of apoptotic bodies, were observed. Other results indicated that the apoptosis induced by the test substance may have been via cell cycle arrest at the G2/M phase.

DERMAL IRRITATION AND SENSITZATION STUDIES

Irritation

In Vitro

Animal

Ammonium Acryloyldimethyltaurate/VP Copolymer

Ammonium Acryloyldimethyltaurate/VP Copolymer (assumed applied neat, not specified) was nonirritating to rabbit skin.[11]

PVP

A 10% PVP-iodine solution did not cause neither dermal irritation in rabbits.[7]

Triacontanyl PVP

The skin irritation potential of a Triacontanyl PVP trade name material (moistened with saline) was evaluated using 6 new Zealand white rabbits.[3] The test substance (0.5 g) was applied, under an occlusive wrap, for 24 h to both an abraded and intact site on each animal. The area (cm^2) of the application site was not stated. Very slight erythema was observed at 2 intact sites and 4 abraded sites (at 24 h) and at 1 intact site and 2 abraded sites (at 72 h). Slight edema was observed at 1 intact site and 2 abraded sites, only at 24 h. The test substance was classified as a slight skin irritant.

VP/VA Copolymer

Acute skin irritation studies of VP/VA Copolymer were conducted on the abraded and intact skin of rabbits. Formulations containing 0.25%-4.0% VP/VA Copolymer produced mild irritation. Solutions of 50% VP/VA in alcohol produced mild irritation, and one sample of the 100% powder moistened in water produced no irritation.[8]

Human

PVP

In 48-h and 96-h Shelanski patch tests, both involving 200 subjects, undiluted PVP-iodine (10% PVP and 2% iodine) was not a skin irritant.[7] *In 3 studies, groups of 20 subjects were patch tested with a foundation containing 2% PVP. One to 2 subjects in each group had minimal faint, uniform or spotty erythema.*

The irritation and sensitization potential of different preparations that contain iodine, including PVP-iodine, was investigated in 24 fair-skinned, healthy subjects without a history of iodine allergy.[34] *PVP-iodine was tested at concentrations of 1%, 5%, 7.5%, and 10% on the intrascapular area on the back or on the volar forearm (2-day application) with Finn Chambers on Scanpor tape. Only 1 subject reacted to PVP-iodine, at concentrations of 7.5% (vesiculation on day 4) and 10% (definite erythema on day 4).*

VP/VA Copolymer

VP/VA Copolymer (50% in alcohol solution, 5 g dose) was mildly irritating to the skin in 24-h patch tests involving groups of 6 rabbits, whereas the undiluted ingredient was nonirritating to the skin of 6 rabbits.[8] *In 24-h skin irritation tests, using groups of 3 to 9 rabbits, on product formulations containing various concentrations of VP/VA Copolymer, concentrations of 0.5%, 1.50% and 4% were nonirritating and a test concentration of 1.75% had the potential for minimal irritation.*

Sensitization

Animal

Ammonium Acryloyldimethyltaurate/VP Copolymer

Ammonium Acryloyldimethyltaurate/VP Copolymer (neat) was not sensitizing to guinea pigs.[11]

PVP

A 10% PVP-iodine solution did not cause dermal sensitization in rabbits.[7]

Sodium Acryloyldimethyltaurate/VP Crosspolymer

The skin sensitization potential of Sodium Acryloyldimethyltaurate/VP Crosspolymer was evaluated in the LLNA (OECD TG 429).[5] There was no evidence of sensitization.

VP/VA Copolymer

VP/VA Copolymer was not a sensitizer to guinea pigs after repeated intracutaneous injections.[8] *The skin was inspected 24 h after each injection.*

Human

PVP

Undiluted PVP-iodine (10% PVP, 2% iodine) did not induce sensitization in an HRIPT involving 100 subjects.[7] *In an exaggerated use study (Draize-Shelanski patch test technique) on a PVP trade name material (PVP concentration not stated) involving 150 subjects, results were negative for skin sensitization*. *Results were also negative in an HRIPT (27 subjects) on a PVP trade name material (10% aqueous solution). In a maximization test involving 25 subjects, 2% PVP did not induce contact allergy*.

Triacontanyl PVP

The skin sensitization potential of a Triacontanyl PVP trade name material was evaluated in an HRIPT involving 102 subjects (21 males, 81 females).[3] Nine 24-h induction patches (type not stated), each containing ~200 mg of the test substance, were applied to the left upper back of each subject over a 3-week period. The area of application (cm^2) was not stated. A 24-h challenge patch was applied 2 weeks after removal of the last induction patch. Reactions were scored at 48 h and 72 h post-application. A minimal reaction (not defined) was observed in 6 subjects during the induction phase. Reactions were not observed during the challenge phase. The test substance was a non-sensitizer.

VP/Acrylates/Lauryl Methacrylate Copolymer

In an HRIPT involving 105 subjects, VP/Acrylates/Lauryl Methacrylate Copolymer (96%) induced minimal erythema in 6 and 2 subjects during the induction and challenge phases, respectively.[4] These results were not considered positive by the authors of this study. Details relating to the test protocol were not included.

VP/VA Copolymer

Repeated insult patch tests of a 5.0% formulation of VP/VA Copolymer caused no irritation or sensitization in 50 subjects. Likewise, three solutions of 50% PVP/VA Copolymer in alcohol caused no irritation in 150 subjects.[8]

Photosensitization/Phototoxicity

Animal

VP/VA Copolymer

No photosensitization data on VP/VA Copolymer were available for review, but the UV absorption characteristics suggest that photosensitization is unlikely.[8]

Human

PVP

A PVP trade name material (10% aqueous solution) did not induce a phototoxic response in a study involving 10 human subjects.[7]

Triacontanyl PVP

The phototoxicity of a Triacontanyl PVP trade name material was evaluated using 10 subjects (1 male, 9 females). The test substance (~200 mg) was applied, under an occlusive wrap, for 24 h to both forearms of each subject.[3] The area of application (cm^2) was not stated. After removal of the occlusive wrap, 1 forearm of each subject was irradiated with UVA light. Both arms of each subject were evaluated for reactions on days 2, 3, and 4, and reactions were not observed. The test substance did not induce a contact dermal phototoxic response.

During the induction phase of a photoallergenicity study, a Triacontanyl PVP trade name material (200 mg) was applied, under an occlusive wrap, for 24 h to both forearms of 28 subjects.[3] The area of application (cm^2) was not stated. The study involved a 3-week induction phase, 2-week non-treatment period, and then a challenge phase. After 24 h, the occlusive wraps were removed and 1 forearm of each subject was irradiated for 15 minutes with UVA light (3.3 joules) and UVB light (108 to 144 m Joules). Induction was repeated 6 times during a 3-week period. The challenge phase began 2 weeks after the last induction (followed by irradiation). The test substance was applied (under an occlusive wrap) for 24 h to a new site on the forearm. After removal of the occlusive wrap, 1 forearm was irradiated with UVA light. Test sites were evaluated immediately after irradiation and at 48 h and 72 h post-application. A challenge reaction (minimal reaction) was observed in 1 subject, only at the site that was irradiated after test substance application. The test substance did not induce contact photoallergy.

OCULAR IRRITATION STUDIES

In Vitro

PVP

PVP-iodine was severely toxic to corneal endothelium at concentrations of 5% and 10% in a rabbit eye model.[34] *An in vitro study of cultured bovine corneal endothelial cells with PVP-iodine concentrations up to 0.1% found that concentrations of 0.05% or less did not induce endothelial cell damage.*[34]

Animal

Ammonium Acryloyldimethyltaurate/VP Copolymer

In an ocular irritation assay, Ammonium Acryloyldimethyltaurate/VP Copolymer was nonirritating to the eyes of rabbits.[35]

PVP

In ocular irritation studies using rabbits, a 10% PVP-iodine solution (without detergent) was minimally toxic, whereas repeated instillations of 0.5% PVP-iodine did not cause ocular irritation.[7]

An in vivo study on rabbits with PVP-iodine up to 1% found concentrations of 0.1% or less did not damage the corneal endothelium.[34]

Sodium Acryloyldimethyltaurate/VP Crosspolymer

The ocular irritation potential of Sodium Acryloyldimethyltaurate/VP Crosspolymer (test concentration unknown) was evaluated using rabbits in accordance with OECD TG 405.[5] Slight conjunctival effects were observed and had resolved by 24 h. The test substance was classified as slightly irritating.

VP/Acrylates/Lauryl Methacrylate Copolymer

Undiluted VP/Acrylates/Lauryl Methacrylate Copolymer was slightly irritating to the eyes of rabbits.[4] The number of animals tested and details relating to the test protocol and study results are not included.

VP/VA Copolymer

The acute ocular irritation of VP/VA Copolymer, as supplied, and in formulation, was tested on albino rabbits. Solutions of 25%-50% VP/VA in alcohol produced no reaction to severe irritation. Formulations containing 2.5%-24% VP/VA Copolymer also produced no reaction or moderate irritation.[8]

Triacontanyl PVP

In a study involving 6 New Zealand white rabbits, a Triacontanyl PVP trade name material was instilled (50 mg) into the conjunctival sac (1 eye) of each animal.[3] Untreated eyes served as controls. The eyes of 3 rabbits were rinsed after instillation. Reactions were scored for up to 7 days post-instillation according to the Draize scale. In all treated eyes, slight erythema, edema, and discharge were observed at 1 h post-instillation. Conjunctival irritation persisted for 4 days in 1 eye (unrinsed) and, for 1 day, in 1 rinsed eye. The test substance was classified as a slight ocular irritant.

CLINICAL STUDIES

Case Reports

PVP

A woman with pollinosis developed anaphylaxis after vaginal application of a PVP-iodine solution for disinfection during a medical examination.[34] Wheal and flare responses (3+) to the PVP-iodine solution (10% aq.), PVP-iodine (0.1% aq.) and PVP (0.001% aq.) were observed following prick tests. In another case study, a man had an anaphylactic reaction minutes after oral ingestion of acetaminophen-containing tablets.[34] A positive test reaction to PVP (5% in water), one of the drug's components, was reported.

A case of a boy with a history of anaphylactic reactions following treatment for impetigo contagiosum was reported.[34] Skin prick tests with PVP-iodine solution (0.1-100 mg/dl in water) and PVP (K30; 0.1-10 mg/ml in water)were negative. However, in a histamine release test (using peripheral blood basophils), histamine release was observed in a dose-dependent manner after stimulation with PVP in the presence of autologous serum. A rare case of iododerma was reported in a man with a history of diabetes, hypertension, asthma, and gout.[34] Treatment with a 10% topical solution of PVP-iodine resulted in multiple pinpoint pustules (consistent with iododerma) on both lower extremities.

Four days following surgery to treat carpal tunnel syndrome, a woman presented with an acute vesicular dermatitis on her left hand, palm and dorsal surface, and interdigital spaces.[34] These reactions were observed after application of a 10% PVP-iodine solution to the surgical site. Patch testing with PVP-iodine solution (1% diluted in water) caused a positive (4+) reaction. A positive reaction (++) was also observed in the repeated open application test (ROAT).

Severe irritant contact dermatitis resulting in necrosis of the skin occurred in a woman following surgical preparation of her chest and upper abdomen with 10% PVP-iodine solution.[34] A woman with no significant medical history developed transient hypotension, anuric renal failure, hemolysis, coagulopathy, and uterine infarction following intra-uterine injection of 2% PVP-iodine solution as a dye in a hydrotubation procedure.[34] In another report, PVP-iodine-induced irritant contact dermatitis was diagnosed in a woman following antiseptic preparation of a spinal anesthesia site for an emergency Caesarean section.[34]

Other Clinical Reports

PVP

In the patch testing of 500 consecutive patients with 10% PVP-iodine solution (diluted 10 times in water), 14 patients (2.8%) had a positive reaction to the test material.[34] These patients then underwent ROATs with a PVP-iodine solution and only 2 of the 14 patients tested positive.

Patch testing was performed on 10 patients with a history of contact dermatitis following application of PVP-iodine preparations and positive patch test reactions to the preparations.[34] On days 3 and 5, "+" reactions or stronger were observed in 10/10 patients with 10% PVP-iodine, in 9/9 patients with 5% PVP-iodine, and in 5/9 patients with 2% PVP-iodine. All patients (10/10) had positive reactions to the PVP-iodine preparation tested neat. In the control group, "+" reactions were observed in 3/10 to 5% and 10% PVP-iodine and to the PVP-iodine preparation. No reactions were observed to lower test concentrations or to any of the other components tested. The strong reactions were classified as allergic sensitization.

In a survey of physicians in Japan for occupational allergy, 17 out of 307 reported contact allergy to PVP-iodine.[34]

Nineteen patients (12 men and 7 women) developed extensive patchy or linear erythema, sometimes accompanied by bullae and erosion, on both sides of the buttocks, the back and posterior areas of the thighs a few days after operations or cardioangiography.[34] The patients were patch tested with 10% PVP-iodine solution and had strongly positive results (irritant contact dermatitis).

VP/Eicosene Copolymer

An atopic male with a history of xerosis and pruritus of the hands, lower arms, and legs applied a prescribed emollient cream containing VP/Eicosene Copolymer (concentration not stated) daily.[36] Within a month, the patient developed an itchy, vesicular dermatitis of the limbs. Patch testing of the cream was performed, and reactions were scored on days 2 and 3. A mild erythemato-edematous (+) reaction to the cream was observed on both days. In a repeated open application test in which the cream was applied to the antecubital fossa, a positive reaction was observed within 3 days. At 6 months after resolution of the dermatitis, the patient was patch tested with the cream and its ingredients. Reactions were scored on days 2, 3, and 4. A delayed, but clearly positive, erythemato-edematous reaction (+ reaction) to 10% VP/Eicosene Copolymer in petrolatum was observed on day 4. A positive reaction to the cream (+/+) was observed on days 3 and 4. The patch test reaction to VP/Eicosene Copolymer was considered allergic and clinically relevant. Positive reactions were not observed in the 15 control subjects patch tested with VP/Eicosene Copolymer.

Acute facial eczema was observed in a female patient after application of a sunscreen containing VP/Eicosene Copolymer (concentration not stated) and 23 other ingredients.[37] Product application was followed by moderate sun exposure. The patient had a childhood history of eczema. One month later, patch testing (Finn chambers, applied to back) of the ingredient and product was performed. Reactions were scored after days 2 and 3, and a positive reaction (+/+) to the sunscreen was observed. In a second patch test on the sunscreen, the test site was irradiated with UVA (10 J/cm^2) on day 2. A positive reaction was observed on days 2 and 3 (+/+). Patch testing of the individual ingredients was also performed, and test results indicated that VP/Eicosene Copolymer was the only ingredient that caused a positive reaction. A positive reaction to this ingredient (1% in petrolatum) was observed on days 2 and 3 (+/+).

SUMMARY

The safety of 30 vinylpyrrolidone polymers as used in cosmetics is being reviewed in this safety assessment. Most of these ingredients have the film former function in cosmetics in common. Viscosity increasing agent and binder are 2 other functions that are frequently being reported.

VP/VA Copolymer is produced by free radical copolymerization of N-vinyl-2-pyrrolidone (NVP) and vinyl acetate (VA) in solution in isopropanol, in the presence of initiators. The process is continuous and temperature-controlled. Hydrazine is formed from amines present in this reaction mixture. Some of the proposed specifications for VP/VA Copolymer, as a food ingredient, in a petitioner's submission to the EFSA are: vinylpyrrolidone (5 mg/kg maximum), vinyl acetate (5 mg/kg maximum), and hydrazine (1 mg/kg maximum).

Maltodextrin/VP Copolymer contains an unnamed low molecular weight species that is <1000 Da (0.8% of composition) and an unnamed low molecular weight species that is < 500 Da (0.1% of composition). The residual NVP monomer content in the PVP imported into Australia varies and ranges from 10 ppm to 2000 ppm. In Europe, NVP residues in PVP are generally below 100 ppm.

According to 2018 VCRP data, the greatest use frequency is being reported for PVP, which is being used in 900 cosmetic products (798 leave-on products + 101 rinse-off products + 1 product diluted for bath use). The second highest use frequency (597 cosmetic products: 525 leave-on products + 62 rinse-off products) is being reported for Ammonium Acryloyldimethyltaurate/VP Copolymer. In general, the differences in current use frequencies of vinylpyrrolidone polymers in cosmetics versus those reported in previous years are unremarkable.

The results of a concentration of use survey conducted in 2017 indicate that VP/VA Copolymer is being used at concentrations up to 44% in rinse-off products (paste masks and mud packs), which is the highest maximum ingredient use concentration that is being reported for vinylpyrrolidone polymers. Notably, in 2003, the highest maximum use concentration of VP/VA Copolymer in rinse-off products was 10%, which is 4-fold lower than the current highest maximum use concentration in rinse-off products. The highest maximum ingredient use concentration of vinylpyrrolidone polymers in leave-on products is being reported for PVP, which is being used at concentrations up to 35% in leg and body paints. Notably, in 2013, the highest maximum use concentration of PVP in leave-on products was lower, 12%. Thus, the highest maximum use concentration of PVP in leave-on products is approximately 3-fold greater than the highest maximum use concentration of this ingredient in leave-on products that was reported in 2013.

The absorption, distribution, metabolism, and excretion of PVP is dependent on molecular weight, amount and frequency of dosing, and route of administration. Polymers with a weight < 25,000 Da are eliminated through the kidneys. An oral dosing study using 0.9 mg per rat of a PVP trade name material found no significant absorption. After subcutaneous injection, VP/VA Copolymer was stored in the spleen, the liver, kidneys, lung, and bone marrow. Some of the copolymer was excreted in the urine.

A single dose of a Triacontanyl PVP trade name material was applied, under an occlusive wrap, for 24 h to the backs of 10 New Zealand white rabbits. None of the animals died, no abnormal clinical signs were observed, and the acute dermal LD_{50} was > 2 g/kg. An oral LD_{50} of > 5 g/kg (rats) has been reported for undiluted VP/Acrylates/Lauryl Methacrylate Copolymer. Dyspnea was observed in 1 animal.

The acute i.p. toxicity of PVP amphiphilic polymers and polymeric nanoparticles was evaluated using groups of 8 BALB/C mice and groups of 6 Wistar rats. Unassociated polymer solutions or polymer nanoparticles preparations were administered at doses 1 mg/kg to 50 mg/kg body weight (for polymers) and 500 mg/kg to 6000 mg/kg (for nanoparticles). For rats and mice, dosing with the 3 PVP polymers did not result in death, toxicity, or other negative symptoms. For the 3 types of PVP nanoparticles, LD_{50} values for rats and mice were in the 3000 to 5500 mg/kg range (practically nontoxic substances).

VP/VA Copolymer was administered in the diet of 3 groups of male and female Sprague-Dawley rats (5 animals/sex/group) for 28 days at doses up to 1000 mg/kg/day. There were no clinical signs of toxicity or test substance-related macroscopic or microscopic tissue changes. The short-term (28 days) oral toxicity of a PVP trade name material (5% w/v in water) was evaluated using 2 groups of 6 HanWistar rats (RccHan:WIST strain). There were no toxicologically relevant effects on body weight gain, food consumption, or water consumption, and there were no treatment-related microscopic changes.

In a 90-day study, VP/VA Copolymer was also administered in the diet of 3 groups of male and female Sprague-Dawley rats (10 animals/sex/group) for at doses up to 1000 mg/kg/day, respectively. There were no clinical signs of toxicity or test substance-related macroscopic or microscopic tissue changes.

The chronic oral toxicity of VP/VA Copolymer was evaluated using groups of 100 male and female Wistar rats of the Chbb:THOM (SPF) strain. The groups were fed the test substance (in the diet) for 2 years, and 2759 mg/kg/day was the highest dose that was administered. There were no effects on survival and no remarkable test substance-related clinical signs in any of the dose groups. The vast majority of the gross lesions were comparable to the incidence in controls, and there was no clear dose-response relationship. A 2-year feeding study on VP/VA Copolymer (5% in diet) was also performed using groups of 102 Sprague-Dawley rats. Survival in both the control and test groups was described as poor (8% to 14%), due to inflammatory diseases of the respiratory tract. There were no signs of toxicity in test or control rats, and no treatment-related clinical chemistry changes. No gross pathologically detectable lesions were observed. However, at microscopic examination, an increased incidence of liver congestion and fatty degeneration was observed.

In a chronic (52 weeks) feeding study, groups of 8 to 12 dogs were fed VP/VA Copolymer in the diet, and 2522 mg/kg/day was the highest dose that was administered. None of the animals died and no treatment-related clinical signs were observed. At gross and microscopic examinations, the type and incidence of findings were comparable between test and control groups.

The genotoxicity of 10% aqueous PVP was evaluated in the Ames test (with and without metabolic activation) using the *Salmonella typhimurium* TA98, TA100, TA1535, and TA1537. Results were negative. Sodium Acryloyldimethyltaurate/VP Crosspolymer was also non-genotoxic (doses not stated) in the Ames test, and the same was true for a Triacontanyl PVP trade name material (doses up to 2500 µg/plate, with and without metabolic activation).

The carcinogenicity of VP/VA Copolymer was evaluated using groups of 100 male and female Wistar rats of the Chbb:THOM (SPF) strain. The groups were fed the test substance (in the diet) for 2 years, and 2759 mg/kg/day was the highest dose that was administered. All neoplastic and non-neoplastic microscopic findings were considered to have developed spontaneously and were not related to treatment. A 2-year feeding study on VP/VA Copolymer (5% in diet) was also performed using groups of 102 Sprague-Dawley rats. No treatment-related tumors or other gross pathologically detectable lesions were induced.

A Triacontanyl PVP trade name material (0.5 g, moistened with saline) was slightly irritating to the skin of 6 New Zealand white rabbits. Formulations containing 1.75%, 4%, and 5% VP/VA Copolymer produced no irritation in 24-hour patch tests.

Results for Sodium Acryloyldimethyltaurate/VP Crosspolymer were negative in the LLNA. The skin sensitization potential of a Triacontanyl PVP trade name material (~200 mg) was evaluated in an HRIPT involving 102 subjects, and results were negative. In an HRIPT involving 105 subjects, VP/Acrylates/Lauryl Methacrylate Copolymer (96%) induced minimal erythema in 6 and 2 subjects during the induction and challenge phases, respectively. These reactions were not considered positive.

In a study involving 10 subjects, a Triacontanyl PVP trade name material (~200 mg) did not induce a contact dermal phototoxic response in the presence of UVA light. During the induction phase of a photoallergenicity study, a Triacontanyl PVP trade name material (200 mg) was applied to the forearms of 28 subjects. A challenge reaction (minimal reaction) was observed in 1 subject, only at the site that was irradiated after test substance application. It was concluded that the trade name material did not induce contact photoallergy.

An unknown concentration of Sodium Acryloyldimethyltaurate/VP Crosspolymer was classified as slightly irritating to the eyes of rabbits. Undiluted VP/Acrylates/Lauryl Methacrylate Copolymer was also slightly irritating to the eyes of rabbits. In a study involving 6 New Zealand white rabbits, a Triacontanyl PVP trade name material (50 mg) was classified as slightly irritating.

An allergic (erythemato-edematous) reaction was observed in an atopic patient patch-tested with 10% VP/Eicosene Copolymer in petrolatum, but not in 15 control subjects. Acute facial eczema was observed in a female patient after application of a sunscreen containing VP/Eicosene Copolymer (concentration not stated). When the patient was patch-tested with the ingredient (1% in petrolatum), a positive reaction was observed.

DATA NEEDS

1. Method of manufacture and impurities data
2. Chemical characterization data
3. Additional irritation and sensitization data at concentration of use, especially for those ingredients for which this information is absent

TABLES

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1; CIR Staff] *

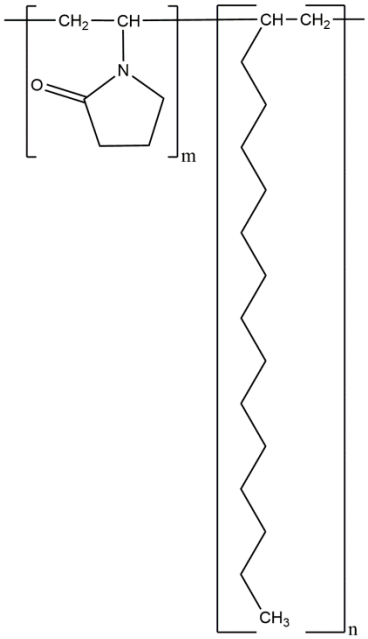
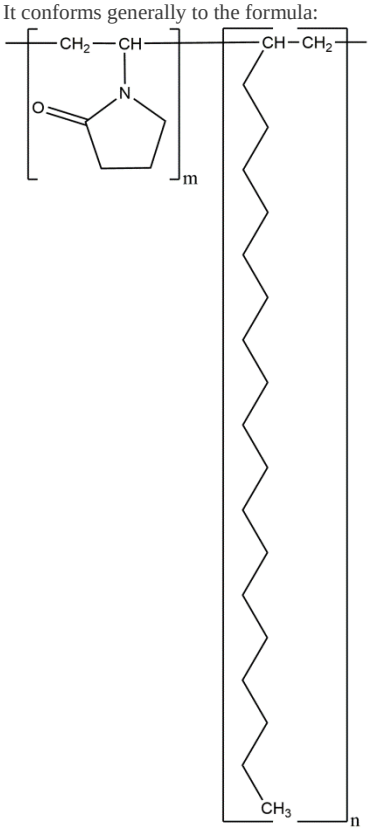
Ingredient CAS No.	Definition & Structures	Function(s)
VP/Hexadecene Copolymer 32440-50-9 63231-81-2	VP/Hexadecene Copolymer is a polymer of hexadecene and vinylpyrrolidone monomers 	Binders; Dispersing Agents - Nonsurfactant; Film Formers; Hair Fixatives; Viscosity Increasing Agents - Nonaqueous
VP/Eicosene Copolymer 28211-18-9 77035-98-4	VP/Eicosene Copolymer is a polymer of vinylpyrrolidone and eicosene monomers. It conforms generally to the formula: 	Binders; Dispersing Agents - Nonsurfactant; Film Formers; Viscosity Increasing Agents - Nonaqueous

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1; CIR Staff] *

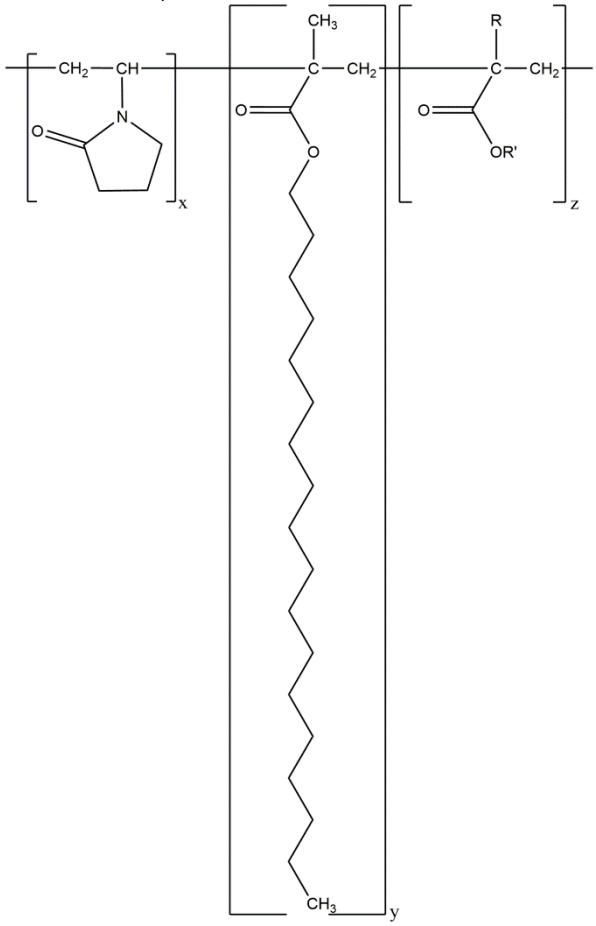
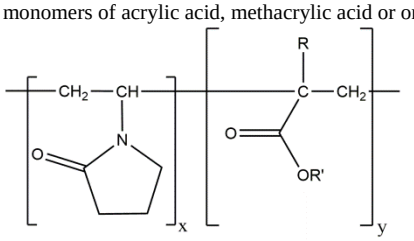
Ingredient CAS No.	Definition & Structures	Function(s)
Acrylates/Stearyl Methacrylate/VP Copolymer	Acrylates/Stearyl Methacrylate/VP Copolymer is a copolymer of vinylpyrrolidone, stearyl methacrylate, and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters.  [wherein R is methyl or hydrogen and R' is hydrogen, methyl, ethyl, propyl, or butyl]	Emulsion Stabilizers; Film Formers; Hair Fixatives; Viscosity Increasing Agents - Aqueous
Acrylates/VP Copolymer 26589-26-4	Acrylates/VP Copolymer is a copolymer of *N*-vinyl pyrrolidone and one or more monomers of acrylic acid, methacrylic acid or one of their simple esters.  [wherein R is methyl or hydrogen and R' is hydrogen, methyl, ethyl, propyl, or butyl]	Binders; Dispersing Agents - Nonsurfactant; Film Formers; Hair Fixatives

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1; CIR Staff] *

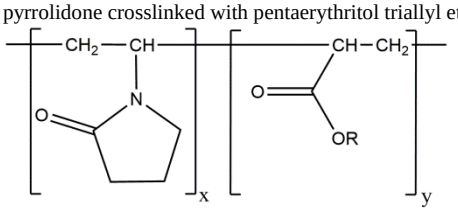
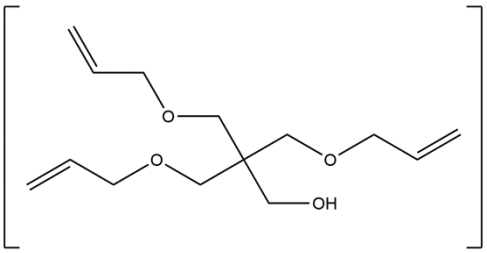
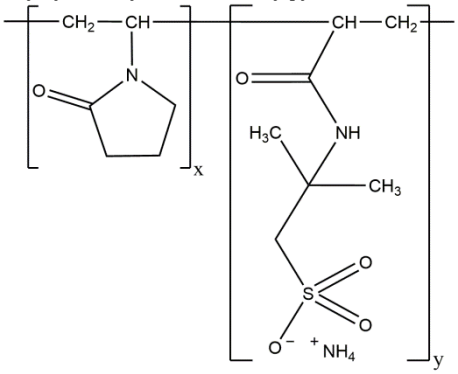
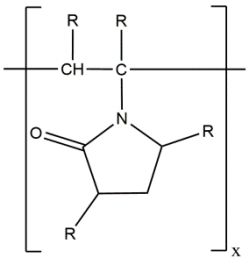
Ingredient CAS No.	Definition & Structures	Function(s)
Acrylic Acid/VP Crosspolymer 527685-31-0	Acrylic Acid/VP Crosspolymer is a copolymer of acrylic acid and *N*-vinyl pyrrolidone crosslinked with pentaerythritol triallyl ether (PETE).  [wherein R is hydrogen or a crosslink through PETE]  pentaerythritol triallyl ether	Dispersing Agents - Nonsurfactant; Slip Modifiers; Surface Modifiers
Ammonium Acryloyldimethyltaurate/VP Copolymer	Ammonium Acryloyldimethyltaurate/VP Copolymer is a copolymer of ammonium acryloyldimethyltaurate and vinylpyrrolidone monomers. 	Viscosity Increasing Agents - Aqueous
Butylated PVP	Butylated PVP is a polymer of butylated vinylpyrrolidone that conforms generally to the formula:  where R represents either a butyl group or hydrogen.	Binders; Film Formers; Hair Fixatives

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1; CIR Staff] *

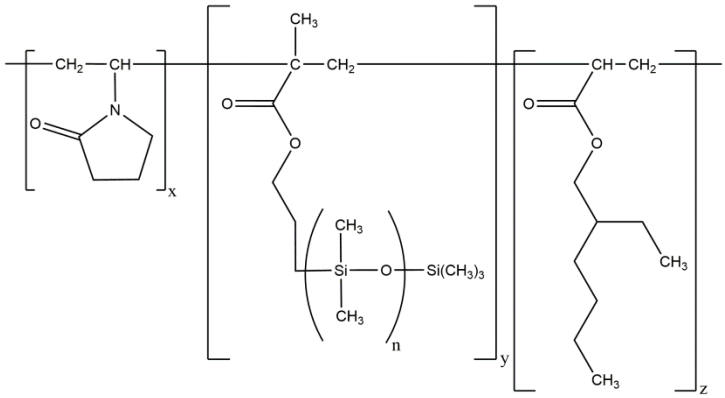
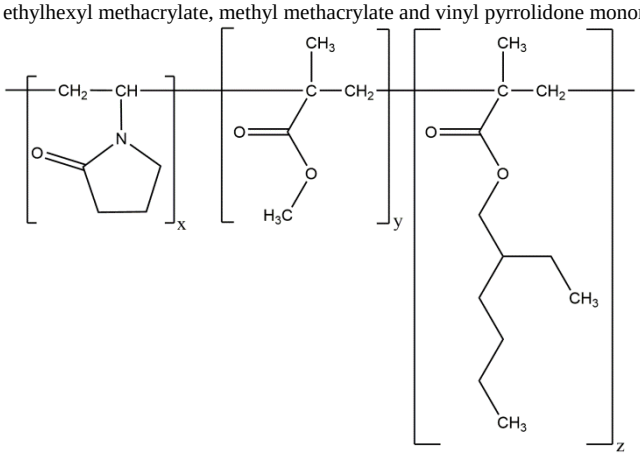
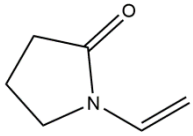
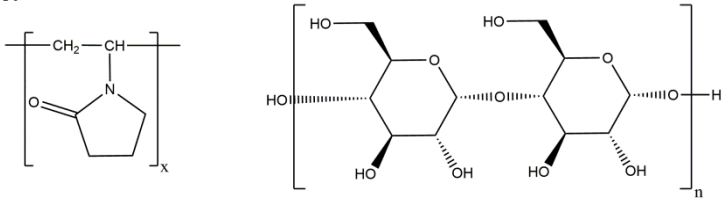
Ingredient CAS No.	Definition & Structures	Function(s)
Ethylhexyl Acrylate/VP/Dimethicone Methacrylate Copolymer	Ethylhexyl Acrylate/VP/Dimethicone Methacrylate Copolymer is a copolymer of vinylpyrrolidone, 2-ethylhexyl acrylate, and dimethicone propylmethacrylate. It conforms to the formula: 	Skin-Conditioning Agents - Miscellaneous; Viscosity Increasing Agents - Nonaqueous
Ethylhexyl Methacrylate/Methyl Methacrylate/VP Copolymer 155532-97-1	Ethylhexyl Methacrylate/Methyl Methacrylate/VP Copolymer is the copolymer of ethylhexyl methacrylate, methyl methacrylate and vinyl pyrrolidone monomers. 	Film Formers
Hydrolyzed Wheat Protein/PVP Crosspolymer	Hydrolyzed Wheat Protein/PVP Crosspolymer is a crosslinked copolymer of hydrolyzed wheat protein and PVP.  [Monomer:] vinylpyrrolidone [The monomer, hydrolyzed wheat protein, is the partial hydrolysate of wheat protein derived by acid, enzyme or other method of hydrolysis.]	Film Formers; Hair Conditioning Agents; Hair Fixatives; Skin-Conditioning Agents - Miscellaneous
Maltodextrin/VP Copolymer 1323833-56-2	Maltodextrin/VP Copolymer is a copolymer of Maltodextrin and vinyl pyrrolidone. 	Film Formers

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1; CIR Staff] *

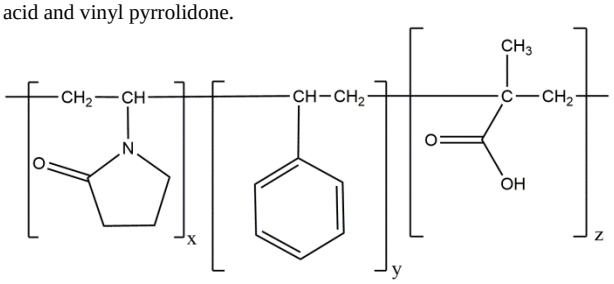
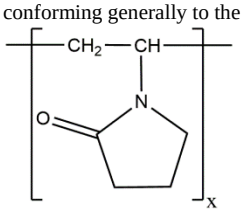
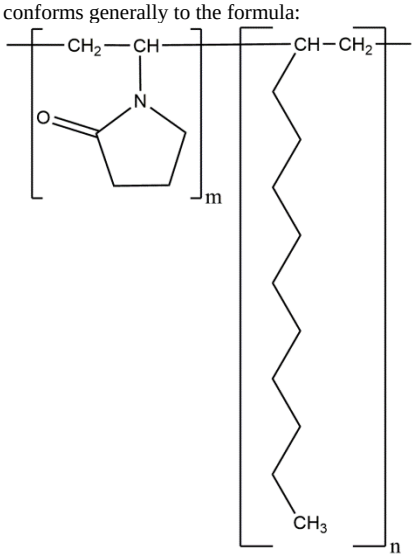
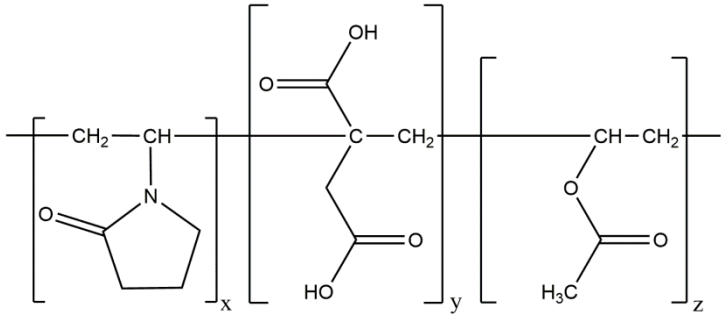
Ingredient CAS No.	Definition & Structures	Function(s)
Methacrylic Acid/Styrene/VP Copolymer 27554-92-3	Methacrylic Acid/Styrene/VP Copolymer is a copolymer of styrene, methacrylic acid and vinyl pyrrolidone. 	Opacifying Agents
PVP 9003-39-8	PVP is the linear polymer that consists of 1-vinyl-2-pyrrolidone monomers conforming generally to the formula: 	Binders; Dispersing Agents - Nonsurfactant; Emulsion Stabilizers; Film Formers; Hair Fixatives
PVP/Decene Copolymer	PVP/Decene Copolymer is a polymer of vinylpyrrolidone and decene monomers. It conforms generally to the formula: 	Binders; Emulsion Stabilizers; Viscosity Increasing Agents - Aqueous; Viscosity Increasing Agents - Nonaqueous
PVP/VA/Itaconic Acid Copolymer 68928-72-3	PVP/VA/Itaconic Acid Copolymer is a polymer formed from vinylpyrrolidone, vinyl acetate and itaconic acid monomers. 	Binders; Dispersing Agents - Nonsurfactant; Film Formers; Hair Fixatives

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1; CIR Staff] *

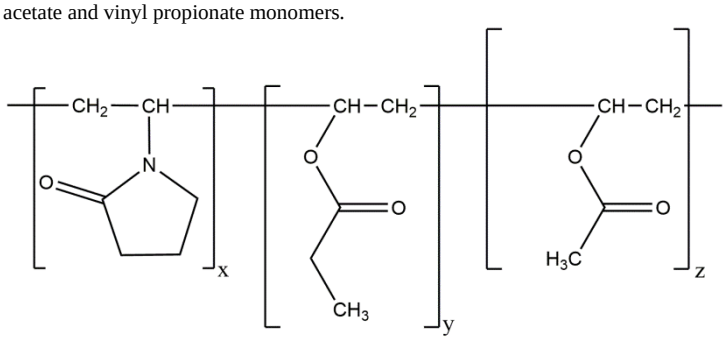
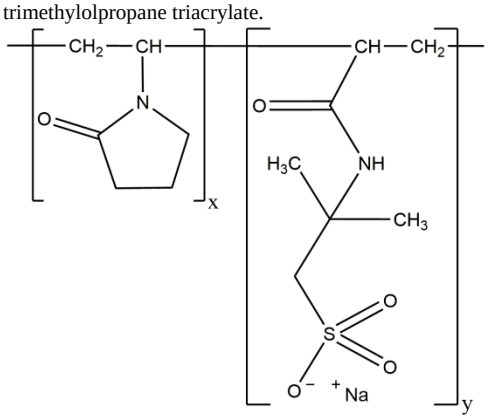
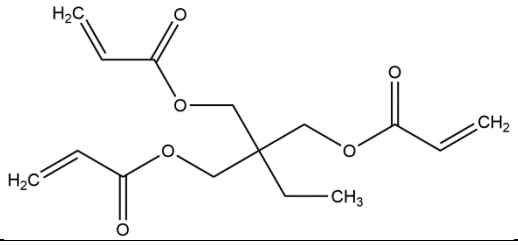
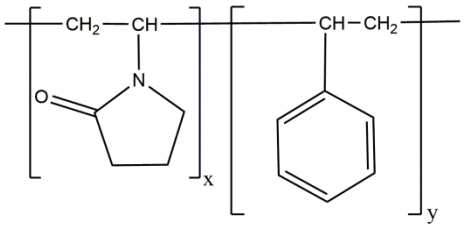
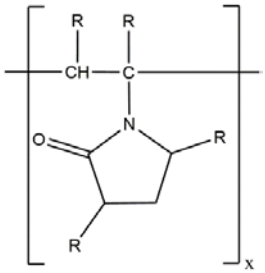
Ingredient CAS No.	Definition & Structures	Function(s)
PVP/VA/Vinyl Propionate Copolymer	PVP/VA/Vinyl Propionate Copolymer is a polymer of vinylpyrrolidone, vinyl acetate and vinyl propionate monomers. 	Film Formers; Hair Fixatives
Sodium Acryloyldimethyltaurate/VP Crosspolymer	Sodium Acryloyldimethyltaurate/VP Crosspolymer is a copolymer of sodium acryloyldimethyltaurate and vinylpyrrolidone crosslinked by 1,1,1-trimethylolpropane triacrylate.  [crosslinked with] 	Emulsion Stabilizers
Styrene/VP Copolymer 25086-29-7	Styrene/VP Copolymer is a copolymer prepared from vinylpyrrolidone and styrene monomers. 	Film Formers
Triacontanyl PVP 157148-07-7 136445-69-7	Triacontanyl PVP is a polymer of vinyl pyrrolidone and 1-triacontene. It conforms to the formula: 	Film Formers; Viscosity Increasing Agents - Nonaqueous

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1; CIR Staff] *

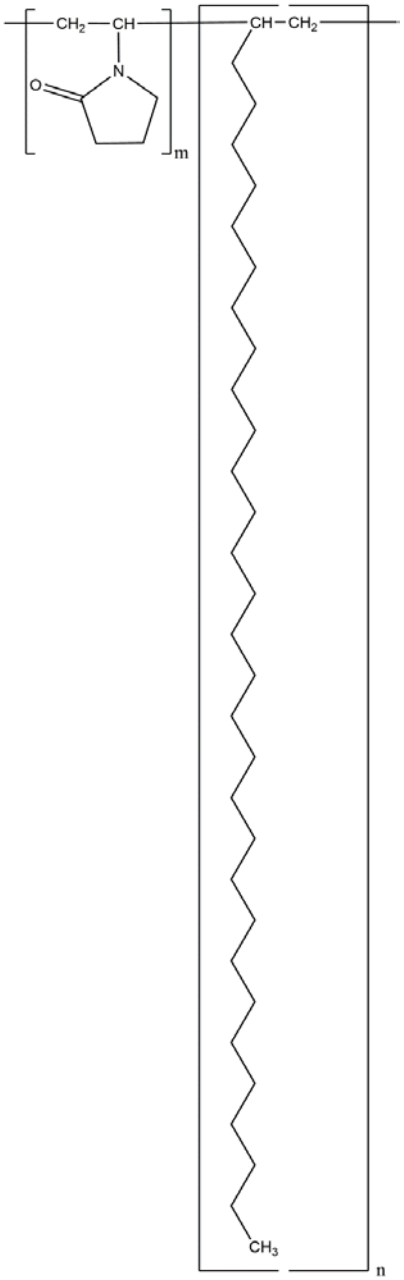
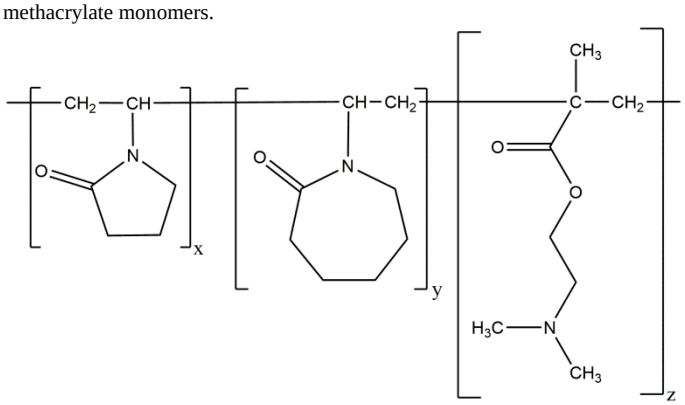
Ingredient CAS No.	Definition & Structures	Function(s)
Triacontene/VP Copolymer	Triacontene/VP Copolymer is a copolymer of triacontene and vinylpyrrolidone monomers. 	Emulsion Stabilizers; Film Formers
Vinyl Caprolactam/VP/Dimethylaminoethyl Methacrylate Copolymer	Vinyl Caprolactam/VP/Dimethylaminoethyl Methacrylate Copolymer is a copolymer of vinylcaprolactam, vinylpyrrolidone, and dimethylaminoethyl methacrylate monomers. 	Film Formers; Hair Fixatives

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1; CIR Staff] *

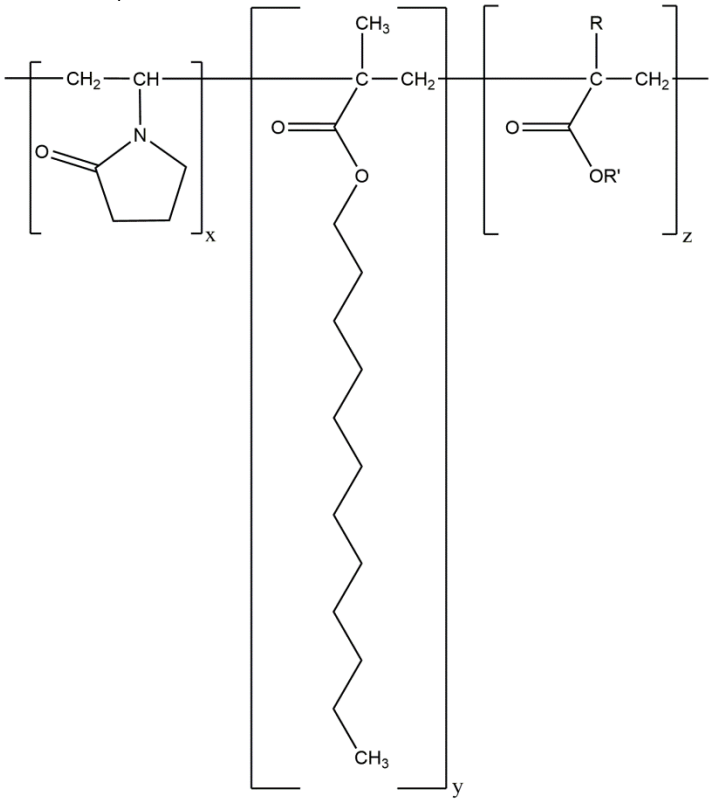
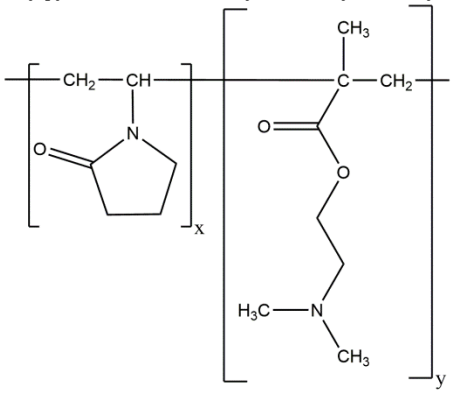
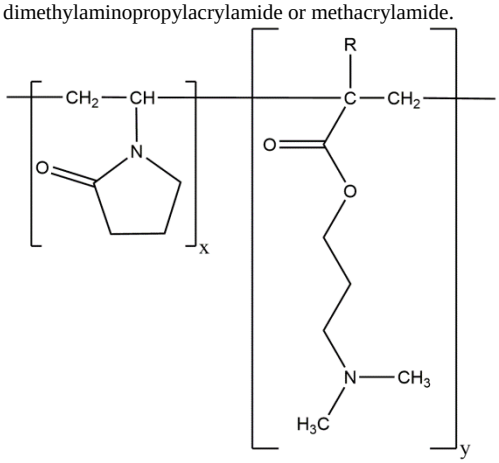
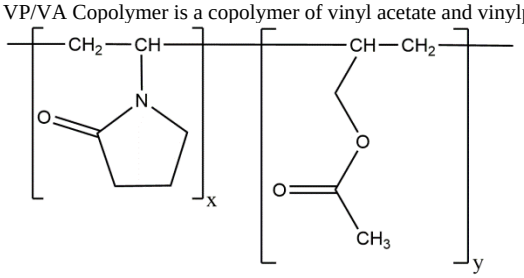
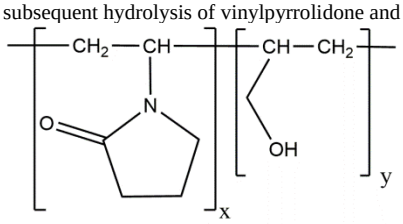
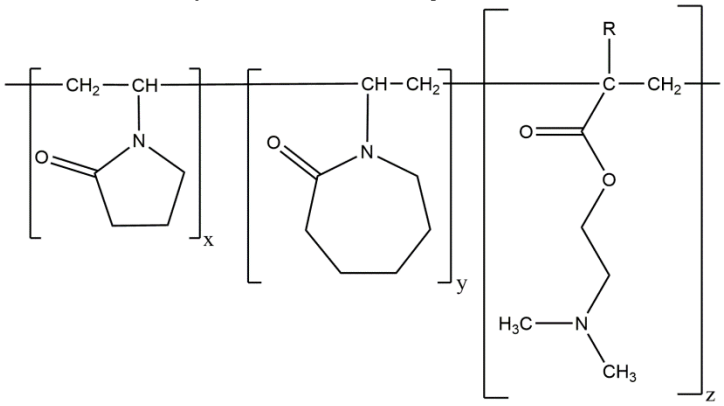
Ingredient CAS No.	Definition & Structures	Function(s)
VP/Acrylates/Lauryl Methacrylate Copolymer 83120-95-0	VP/Acrylates/Lauryl Methacrylate Copolymer is a copolymer of vinylpyrrolidone, lauryl methacrylate, and one or more monomers of acrylic acid, methacrylic acid or one of its simple esters.  [wherein R is methyl or hydrogen and R' is hydrogen, methyl, ethyl, propyl, or butyl]	Hair Fixatives
VP/Dimethiconylacrylate/ Polycarbamyl/Polyglycol Ester	VP/Dimethiconylacrylate/Polycarbamyl/Polyglycol Ester is a copolymer of vinylpyrrolidone, acrylated dimethiconol and polyurethane. [*More information needed to depict structure.*]	Film Formers
VP/Dimethylaminoethylmethacrylate Copolymer 30581-59-0	VP/Dimethylaminoethylmethacrylate Copolymer is a polymer prepared from vinylpyrrolidone and dimethylaminoethylmethacrylate monomers. 	Binders; Dispersing Agents - Nonsurfactant; Film Formers; Hair Fixatives
VP/Dimethylaminoethylmethacrylate/Poly-carbamyl Polyglycol Ester	VP/Dimethylaminoethylmethacrylate/Polycarbamyl Polyglycol Ester is a copolymer of vinylpyrrolidone, dimethylaminoethylmethacrylate and polyurethane. [*More information needed to depict structure.*]	Film Formers

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.[1; CIR Staff] *

Ingredient CAS No.	Definition & Structures	Function(s)
VP/DMAPA Acrylates Copolymer 175893-71-7	VP/DMAPA Acrylates Copolymer is a copolymer of vinylpyrrolidone and dimethylaminopropylacrylamide or methacrylamide.  [wherein R is hydrogen or methyl]	Hair Fixatives
VP/Polycarbamyl Polyglycol Ester	VP/Polycarbamyl Polyglycol Ester is a copolymer of vinylpyrrolidone and polyurethane. [*More information needed to depict structure.*]	Film Formers
VP/VA Copolymer 25086-89-9	VP/VA Copolymer is a copolymer of vinyl acetate and vinylpyrrolidone monomers. 	Binders; Dispersing Agents - Nonsurfactant; Film Formers; Hair Fixatives
VP/Vinyl Alcohol Copolymer 26008-54-8	VP/Vinyl Alcohol Copolymer is the product formed by the polymerization and subsequent hydrolysis of vinylpyrrolidone and vinyl acetate. 	Film Formers; Hair Fixatives; Humectants; Viscosity Increasing Agents - Aqueous
VP/Vinyl Caprolactam/DMAPA Acrylates Copolymer	VP/Vinyl Caprolactam/DMAPA Acrylates Copolymer is a copolymer of vinylpyrrolidone, vinyl caprolactam, dimethylaminopropylacrylamide, and one or more monomers of acrylic acid or one of their simple esters.  [wherein R is hydrogen or methyl]	Hair Fixatives

*Please note: For the sake of simplicity, these ingredients have only been drawn as simple block co-polymers. The periodicity and pattern of interconnectivity between each monomer may vary significantly per ingredient.

Table 2. Published Reports on Similar Ingredients Reviewed by CIR

Ingredients	CIR Review Status
Acrylates/VP Copolymer and VP/Dimethylaminoethylmethacrylate Copolymer	Published Final Report (2002) - Conclusion: Safe for use in cosmetics when formulated to avoid skin irritation.[10] A rereview of this safety assessment is in progress.
Ammonium Acryloyldimethyltaurate/VP Copolymer and Sodium Acryloyldimethyltaurate/VP Crosspolymer	Final Report (issued in 2017) - Conclusion: Safe in cosmetics in the present practices of use and concentration described in this safety assessment.[11]
Methacrylic Acid/Styrene/VP Copolymer and Styrene/VP Copolymer	Final Report (issued in 2014) - Conclusion: Safe in the present practices of use and concentration in cosmetics, as described in this safety assessment.[12]
PVP	Published Final Report (2017) - Conclusion: Safe as used in cosmetics.[7] Published Rereview (2018) - Conclusion: Panel reaffirmed the original conclusion[34]
VP/VA Copolymer	Published Final Report (1983) - Conclusion: Safe as a cosmetic ingredient under present conditions of concentration and use.[8] Published Rereview (2006) - Conclusion: The Panel reaffirmed the original conclusion [14]

Table 3. Monomer Components of Vinylpyrrolidone Polymers

Monomer	CIR Review Status
Acrylated Dimethiconol	Not reviewed
Acrylic Acid	Not reviewed. However, data on this monomer are summarized in the published (2002) CIR final report on Acrylates Copolymer.[10]
Ammonium Acryloyldimethyltaurate	Not reviewed
Butylated Vinylpyrrolidone	Not reviewed
Decene	Not reviewed
Dimethicone Propylmethacrylate	Not reviewed
Dimethylaminoethyl Methacrylate	Not reviewed
Dimethylaminopropylacrylamide	Not reviewed
Eicosene	Not reviewed
Ethylhexyl Methacrylate	Not reviewed
Hexadecene	Not reviewed
Hydrolyzed Wheat Protein	Final Report - Conclusion: Safe for use in cosmetics when formulated to restrict peptides to a weight-average MW of 3500 Da or less.[38]
Itaconic Acid	Not Reviewed
Lauryl Methacrylate	Published Final Report - Conclusion: Safe as used in nail enhancement products when skin contact is avoided. Products containing these ingredients should be accompanied with directions to avoid skin contact, because of the sensitizing potential of methacrylates.[39]
Maltodextrin	Final Report - Conclusion: Safe in the present practices of use and concentration in cosmetics, as described in this safety assessment.[40]
Methacrylamide	Not Reviewed
Methacrylic Acid	Published Final Report - Conclusion: Safe as used as a nail primer by trained professionals, but there are insufficient data for retail use by consumers.[41]
Methyl Methacrylate	Scientific Literature Review (SLR) was issued in 2003, but the report was terminated
Polyurethane	Final Report - Conclusion: Safe as used in the present practices of use and concentration described in this safety assessment.[42]
Sodium Acryloyldimethyltaurate	Not Reviewed
Stearyl Methacrylate	Not Reviewed
Styrene	Not Reviewed
Triacontene	Not Reviewed
Vinyl Acetate	Not Reviewed
Vinyl Caprolactam	Not Reviewed
Vinyl Propionate	Not Reviewed
Vinylpyrrolidone	Not Reviewed

Table 4. Chemical and Physical Properties of Vinylpyrrolidone Polymers

Property	Value/Results	Reference
Maltodextrin/VP Copolymer		
Weight average molecular weight (Da)	132,999	2
Number average molecular weight (Da)	21,499	2
Sodium Acryloyldimethyltaurate/VP Crosspolymer		
Form (at 20 ºC and 101.3 kPa)	White powder	5
Particle size (µm)	< 10 (65.4%); < 100 (86.8%)	5
Formula Weight (Da)	>10,000	5
Melting Point (ºC)	Not determined. Decomposes prior to melting	5
Water solubility (mg/l)	Miscible, gel forming. When gel was diluted by further addition of water, low viscosity solution was formed	5
Triacontanyl PVP (trade name material)		
Form	White to off-white solid flakes	3
Particle size distribution (cm^2)	0.25 to 1	3
Molecular weight (Da)	Approximately 70 to 80% of the polymer has a molecular weight of > 1000	3
Maximum percentage of low molecular weight species (molecular weight <1000 Da) (%)	20 to 30	3
Density (kg/m^3)	947	3
Solubility	Insoluble in water, acid or base solutions	3
Partition coefficient	Not applicable, as the polymer is insoluble in water	3
VP/Acrylates/Lauryl Methacrylate Copolymer		
Form	White powder	4
Particle size (µm)	< 10	4
Number average molecular weight (Da)	>10,000	4
Density (kg/m^3)	1000	4
Solubility	Expected to have low water solubility based on high molecular weight and predominantly hydrophobic structure	4
VP/Dimethylaminoethylmethacrylate Copolymer		
Density (g/cm^3)	1.047	6

Table 5. Specifications for VP/VA Copolymer.[9]

Characteristics	Proposed Specifications
K-value (1% solids in aqueous solution)	25.2 to 30.8
pH-value (10% w/w in distilled water)	3 to 7
Vinyl acetate component in copolymer (%)	Maximum: 35.3 to 42.0
Nitrogen content (%)	7 to 8
Loss on drying (%)	Maximum: 5
Residuals	
Aldehydes (as acetaldehyde) (%)	0.2
Vinyl acetate (mg/kg)	Maximum: 5
Vinylpyrrolidone (mg/kg)	Maximum: 5
Hydrazine (mg/kg)	Maximum: 1
Peroxide content (mg/kg)	Maximum: 400
Isopropanol (mg/kg)	Maximum: 150
Arsenic	Maximum: 3
Lead	Maximum: 2
Mercury	Maximum: 1
Cadmium	Maximum: 1
Ash (residue on ignition/sulfated) (%)	0.1

Table 6. Frequency and Concentration of Vinylpyrrolidone Polymers According to Duration and Exposure.

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	VP/Hexadecene Copolymer				**VP/Eicosene Copolymer**			
	2018[15]		**2017[16]**		**2018[15]**		**2017[16]**	
Totals*	**443**		***0.036-24.1***		**378**		***0.11-8***	
Duration of Use								
Leave-On	***442***		***0.036-24.1***		***377***		***0.11-8***	
Rinse-Off	***1***		***2***		***1***		***NR***	
Diluted for (Bath) Use	***NR***		***NR***		***NR***		***NR***	
Exposure Type								
Eye Area	87		0.25-17.2		239		0.44-8	
Incidental Ingestion	268		0.7-24.1		101		0.96-5.6	
Incidental Inhalation-Spray	6;5[a]		NR		NR;6[a]		4.3	
Incidental Inhalation-Powder	3		NR		NR		0.3-0.5	
Dermal Contact	144		0.036-17.2		92		0.11-8	
Deodorant (underarm)	NR		NR		NR		NR	
Hair - Non-Coloring	NR		NR		1		NR	
Hair-Coloring	NR		NR		NR		NR	
Nail	NR		10.3		NR		NR	
Mucous Membrane	268		0.7-24.1		101		0.96-5.6	
Baby Products	NR		NR		NR		2	
	Acrylic Acid/VP Crosspolymer				**Ammonium Acryloyldimethyltaurate/VP Copolymer**			
	2018[15]		**2017[16]**		**2018[15]**	**2017[11]**	**2017[16]**	**2016[11]**
Totals*	**20**		**0.3-1**		**597**	**584**	**0.096-2**	**0.016-3**
Duration of Use								
Leave-On	***20***		***0.3-1***		***535***	***524***	***0.096-2***	***0.016-3***
Rinse-Off	***NR***		***0.5***		***62***	***60***	***0.2-2***	***0.3-1.8***
Diluted for (Bath) Use	***NR***		***NR***		***NR***	***NR***	***NR***	***NR***
Exposure Type								
Eye Area	3		1		60	66	0.5-3	1.4-3
Incidental Ingestion	NR		NR		2	2	1.5	1.5
Incidental Inhalation-Spray	NR;14[a]		0.3-1[a]		1;197[a]	1;199[a]; 205[b]	0.096-1;1.5[a]	0.096-1;0.4[a]
Incidental Inhalation-Powder	NR		NR		3	1;1[c]; 205[b]	NR	0.18-2[c]
Dermal Contact	10		0.5-1		591	579	0.096-3	0.016-3
Deodorant (underarm)	NR		NR		NR	NR	NR	NR
Hair - Non-Coloring	8		0.3-1		NR	NR	0.8	0.4
Hair-Coloring	NR		NR		NR	NR	NR	NR
Nail	1		NR		NR	NR	NR	NR
Mucous Membrane	NR		0.5		7	5	0.25-1.5	1.5
Baby Products	NR		NR		2	1	0.5	NR
	Butylated PVP				**Hydrolyzed Wheat Protein/PVP Crosspolymer**			
	2018[15]		**2017[16]**		**2018[15]**		**2017[16]**	
Totals*	**4**		**NR**		**48**		**0.017-0.45**	
Duration of Use								
Leave-On	***3***		NR		***34***		***0.017-0.45***	
Rinse-Off	***1***		NR		***14***		***NR***	
Diluted for (Bath) Use	***NR***		NR		***NR***		***NR***	
Exposure Type								
Eye Area	NR		NR		23		0.18-0.4	
Incidental Ingestion	NR		NR		NR		NR	
Incidental Inhalation-Spray	NR;2[a]		NR		NR;8[a]		0.017-0.055; 0.088-0.24[a]	
Incidental Inhalation-Powder	NR		NR		NR		NR	
Dermal Contact	NR		NR		7		0.038-0.45	
Deodorant (underarm)	NR		NR		NR		NR	
Hair - Non-Coloring	4		NR		18		0.017-0.24	
Hair-Coloring	NR		NR		1		NR	
Nail	NR		NR		NR		NR	
Mucous Membrane	NR		NR		NR		NR	
Baby Products	NR		NR		NR		NR	

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

[a] It is possible that these products may be sprays, but it is not specified whether the reported uses are sprays.

[b] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

[c] It is possible that these products may be powders, but it is not specified whether the reported uses are powders

NR - no reported use

Table 6. Frequency and Concentration of Vinyl;pyrrolidone Polymers According to Duration and Exposure.

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Maltodextrin/VP Copolymer				**PVP**			
	2018[15]		**2017[16]**		**2018[15]**	**2013**	**2017[16]**	**2013**
Totals*	**3**		**0.35-3**		**900**	**799**	**0.000003-35**	**0.0005-12**
Duration of Use								
Leave-On	***3***		***0.35-3***		***798***	***675***	***0.005-35***	***0.002-12***
Rinse-Off	***NR***		***NR***		***101***	***123***	***0.000003-13.3***	***0.0005-10.5***
Diluted for (Bath) Use	***NR***		***NR***		***1***	***1***	***0.016-3***	***NR***
Exposure Type								
Eye Area	NR		NR		292	222	0.005-12	0.05-12
Incidental Ingestion	NR		NR		43	35	0.065-13.3	0.1-10.5
Incidental Inhalation-Spray	NR;3[a]		0.35		31;283[a]	22	0.6-5;0.5-9[a]	0.002-5
Incidental Inhalation-Powder	NR		NR		NR	NR	0.1	NR
Dermal Contact	NR		0.35		299	186	0.000003-35	0.0005-12
Deodorant (underarm)	NR		NR		NR	NR	0.66	0.5
Hair - Non-Coloring	3		3		378	423	0.0005-9	0.0005-10.5
Hair-Coloring	NR		NR		11	7	1.4-10	1.6-3.3
Nail	NR		NR		NR	1	0.5-5	0.3-5
Mucous Membrane	NR		NR		44	37	0.065-13.3	0.1-10.5
Baby Products	NR		NR		2	1	4.4	NR

	Sodium Acryloyldimethyltaurate/VP Crosspolymer				**Styrene/VP Copolymer**			
	2018[15]	**2017[11]**	**2017[16]**	**2016[11]**	**2018[15]**	**2013[12]**	**2017[16]**	**2013-2014[12]**
Totals*	**9**	**8**	**0.5-1**	**NR**	**70**	**82**	**0.007-0.8**	**0.000038-1**
Duration of Use								
Leave-On	***9***	***8***	***0.5-1***	***NR***	***17***	***30***	***0.012-0.62***	***0.000038-0.4***
Rinse-Off	***NR***	***NR***	***NR***	***NR***	***53***	***52***	***0.007-0.8***	***0.02-1***
Diluted for (Bath) Use	***NR***	***NR***	***NR***	***NR***	***NR***	***NR***	***NR***	***NR***
Exposure Type								
Eye Area	1	1	NR	NR	1	NR	0.038-0.4	0.2-0.4
Incidental Ingestion	NR	NR	NR	NR	NR	1	NR	NR
Incidental Inhalation-Spray	NR;5[a]	4[a];3[b]	NR;0.89-1[a]	NR	3;8[a]	22	NR;0.016-0.2[a]	0.12
Incidental Inhalation-Powder	NR	3[b]	NR	NR	NR	6	NR	0.12-0.2[c]
Dermal Contact	9	8	0.5-1	NR	15	18	0.012-0.62	0.000038-0.4
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	19	36	0.08-0.2	0.032-1
Hair-Coloring	NR	NR	NR	NR	33	25	0.007-0.8	0.04-0.7
Nail	NR	NR	NR	NR	2	2	0.29	NR
Mucous Membrane	NR	NR	NR	NR	3	6	NR	0.057
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Triacontanyl PVP				**Vinyl Caprolactam/ VP/Dimethylaminoethyl Methacrylate Copolymer**			
	2018[15]		**2017[16]**		**2018[15]**		**2017[16]**	
Totals*	**72**		**0.66-7.3**		**70**		**0.3-5**	
Duration of Use								
Leave-On	***72***		***0.66-7.3***		***65***		***0.3-5***	
Rinse-Off	***NR***		***NR***		***5***		***1.2***	
Diluted for (Bath) Use	***NR***		***NR***		***NR***		***NR***	
Exposure Type								
Eye Area	23		0.66-3.2		1		NR	
Incidental Ingestion	31		3-7.3		NR		NR	
Incidental Inhalation-Spray	NR;1[a]		6.3;1.5-4.5[a]		21;35[a]		1;1.2-5[a]	
Incidental Inhalation-Powder	3		NR		NR		NR	
Dermal Contact	24		0.66-2		3		0.3	
Deodorant (underarm)	NR		NR		NR		NR	
Hair - Non-Coloring	1		1.5-6.3		49		1.2-5	
Hair-Coloring	NR		NR		17		1-1.2	
Nail	NR		NR		NR		NR	
Mucous Membrane	31		3-7.3		NR		NR	
Baby Products	NR		NR		NR		NR	

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

[a] It is possible that these products may be sprays, but it is not specified whether the reported uses are sprays.

[b] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

[c] It is possible that these products may be powders, but it is not specified whether the reported uses are powders

NR - no reported use

Table 6. Frequency and Concentration of Vinylpyrrolidone Polymers According to Duration and Exposure.

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	VP/Acrylates/Lauryl Methacrylate Copolymer				**VP/Dimethiconylacrylate/ Polycarbamyl/ Polyglycol Ester**			
	2018[15]		**2017[16]**		**2018[15]**		**2017[16]**	
Totals*	**15**		**0.0097-3.5**		**3**		**0.04-2.5**	
Duration of Use								
Leave-On	***15***		***0.0097-3.5***		***3***		***0.1-2.5***	
Rinse-Off	***NR***		***NR***		***NR***		***0.04***	
Diluted for (Bath) Use	***NR***		***NR***		***NR***		***NR***	
Exposure Type								
Eye Area	NR		0.0097		NR		0.3-2.5	
Incidental Ingestion	NR		NR		NR		NR	
Incidental Inhalation-Spray	1;4[a]		NR;3.5[a]		NR;1[a]		NR; 0.2-0.6[a]	
Incidental Inhalation-Powder	NR		NR		NR		NR	
Dermal Contact	NR		0.0097-3.5		2		0.04-2.5	
Deodorant (underarm)	NR		NR		NR		NR	
Hair - Non-Coloring	15		NR		NR		NR	
Hair-Coloring	NR		NR		NR		NR	
Nail	NR		NR		NR		NR	
Mucous Membrane	NR		NR		NR		NR	
Baby Products	NR		NR		NR		NR	
	VP/Dimethylaminoethylmethacrylate Copolymer				**VP/DMAPA Acrylates Copolymer**			
	2018[15]	**1998[10]**	**2017[16]**	**1984[10]**	**2018[15]**		**2017[16]**	
Totals*	**72**	**43**	**0.04-6**	**5-10**	**31**		**0.08-7.5**	
Duration of Use								
Leave-On	***65***	***37***	***0.2-6***	***NR***	***23***		**1-7.5**	
Rinse-Off	***7***	***6***	***0.04***	***NR***	***8***		***0.08***	
Diluted for (Bath) Use	***NR***	***NR***	***NR***	***NR***	***NR***		***NR***	
Exposure Type								
Eye Area	4	3	0.2-1	NR	NR		NR	
Incidental Ingestion	NR	NR	NR	NR	NR		NR	
Incidental Inhalation-Spray	1;45[a]	NR;21[a]	NR	NR	1;21[a]		NR;1-7.5[a]	
Incidental Inhalation-Powder	NR	NR	NR	NR	NR		NR	
Dermal Contact	6	NR	0.04-1.2	NR	NR		NR	
Deodorant (underarm)	NR	NR	NR	NR	NR		NR	
Hair - Non-Coloring	63	40	0.5-6	NR	27		0.08-7.5	
Hair-Coloring	1	NR	NR	NR	4		NR	
Nail	NR	NR	NR	NR	NR		NR	
Mucous Membrane	NR	NR	NR	NR	NR		NR	
Baby Products	NR	NR	NR	NR	NR		NR	
	VP/Polycarbamyl Polyglycol Ester				**VP/VA Copolymer**			
	2018[15]		**2017[16]**		**2018[15]**	**2002[14]**	**2017[16]**	**2003[14]**
Totals*	**6**		**0.036**		**480**	**210**	**0.001-44**	**0.3-12**
Duration of Use								
Leave-On	***6***		***0.036***		***442***	*181*	***0.001-10***	***0.3-12***
Rinse-Off	***NR***		***NR***		***37***	*29*	***0.07-44***	***3-10***
Diluted for (Bath) Use	***NR***		***NR***		***1***	*NR*	***NR***	***NR***
Exposure Type								
Eye Area	3		0.036		46	10	0.5-10	0.3-9
Incidental Ingestion	NR		NR		NR	NR	0.07-4	NR
Incidental Inhalation-Spray	NR		NR		35;236[a]	27;87[a]	1-10;0.07-9.9[a]	0.5-4;4-12[a]
Incidental Inhalation-Powder	NR		NR		5	NR	NR	NR
Dermal Contact	5		NR		93	15	0.0075-44	0.3-10
Deodorant (underarm)	NR		NR		NR	NR	NR	NR
Hair - Non-Coloring	NR		NR		330	190	1-10	2-12
Hair-Coloring	NR		NR		33	3	0.29-1.5	0.5
Nail	NR		NR		1	NR	0.001	NR
Mucous Membrane	NR		NR		1	NR	0.07-4	NR
Baby Products	NR		NR		NR	NR	NR	NR

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[b] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

[c] It is possible that these products may be powders, but it is not specified whether the reported uses are powders

NR - no reported use

Table 6. Frequency and Concentration of Vinylpyrrolidone Polymers According to Duration and Exposure.

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	VP/Vinyl Caprolactam/DMAPA Acrylates Copolymer				**Acrylates/VP Copolymer**			
	2018[15]		**2017[16]**		**2018[15]**	**1998[10]**	**2017[16]**	**1997[10]**
Totals*	**19**		**0.5-1.4**		**9**	**4**	**0.67-1.5**	**NR**
Duration of Use								
Leave-On	***19***		***0.5-1.4***		**4**	***2***	***0.67-1.5***	**NR**
Rinse-Off	***NR***		***1.4***		**5**	***2***	***0.81***	**NR**
Diluted for (Bath) Use	***NR***		***NR***		**NR**	***NR***	***NR***	**NR**
Exposure Type								
Eye Area	NR		NR		3	NR	NR	NR
Incidental Ingestion	NR		NR		NR	NR	NR	NR
Incidental Inhalation-Spray	19		0.5-1.4		NR	NR;2[a]	0.67-0.95[a]	NR
Incidental Inhalation-Powder	NR		NR		NR	NR	NR	NR
Dermal Contact	NR		NR		2	NR	0.67 -1.5	NR
Deodorant (underarm)	NR		NR		NR	NR	NR	NR
Hair - Non-Coloring	6		1.4		3	4	0.95	NR
Hair-Coloring	13		0.5		1	NR	NR	NR
Nail	NR		NR		NR	NR	NR	NR
Mucous Membrane	NR		NR		NR	NR	NR	NR
Baby Products	NR		NR		NR	NR	NR	NR
	VP/Dimethylaminoethylmethacrylate/ Polycarbamyl/Polyglycol Ester							
	2018[15]		**2017[16]**					
Totals*	**NR**		**5.6**					
Duration of Use								
Leave-On	***NR***		*5.6*					
Rinse-Off	***NR***		*NR*					
Diluted for (Bath) Use	***NR***		*NR*					
Exposure Type								
Eye Area	NR		NR					
Incidental Ingestion	NR		NR					
Incidental Inhalation-Spray	NR		5.6					
Incidental Inhalation-Powder	NR		NR					
Dermal Contact	NR		NR					
Deodorant (underarm)	NR		NR					
Hair - Non-Coloring	NR		5.6					
Hair-Coloring	NR		NR					
Nail	NR		NR					
Mucous Membrane	NR		NR					
Baby Products	NR		NR					

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

[a] It is possible that these products may be sprays, but it is not specified whether the reported uses are sprays.

[b] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

[c] It is possible that these products may be powders, but it is not specified whether the reported uses are powders

NR - no reported use

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