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# Final Report on the Safety Assessment of Vinyl Acetate/ Crotonic Acid Copolymer

**Vinyl Acetate/Crotonic Acid (VA/CA) Copolymer is a polymer formed from vinyl acetate and crotonic acid monomers. VA/CA Copolymer is primarily used as a film forming agent in aerosol hair sprays and other hair preparations.**

**An aqueous solution containing 3.7% VA/CA Copolymer and a hair spray containing 13.75% of the ingredient were relatively harmless when administered to rats in single oral doses of up to 50 ml/kg and 5 g/kg, respectively. These same test materials elicited no skin irritation in rabbits and minimal, transient eye irritation. Hair spray formulations containing 0.86% of the copolymer caused no skin irritation or sensitization when tested in a repeated insult patch test on humans.**

**On the basis of the available information, Vinyl Acetate/Crotonic Acid Copolymer is considered safe as a cosmetic ingredient under present practices of product and concentration use.**

## INTRODUCTION

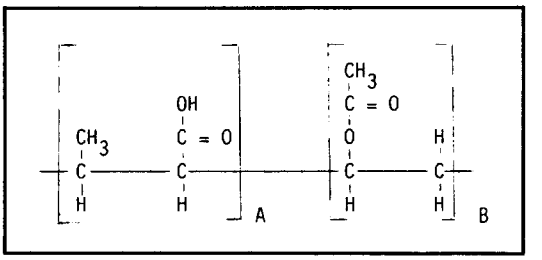
Vinyl Acetate/Crotonic Acid Copolymer is used in cosmetic formulations as the neutralized salt of either AMP (2-amino-2-methyl-1-propanol), AEPD (2-amino-2-ethyl-1,3-propanediol), THMAM (tris hydroxy methyl-amino methane), $NH_3$ (28%), AMPD (2-amino-2-methyl-1,3-propanediol), or morpholine.[1] Despite the reported use of the morpholine salt in cosmetic products, the safety assessment presented here does not pertain to this particular material.

## CHEMICAL AND PHYSICAL PROPERTIES

### Definition and Structure

Vinyl Acetate/Crotonic Acid Copolymer* (CAS No.: 25609-89-6) is a copolymer of vinyl acetate and crotonic acid monomers.[2] The general structural formula is:

*Hereafter referred to as VA/CA Copolymer.




where the number of vinyl acetate monomers (B) is greater than the number of crotonic acid monomers (A). The relative number of molecules of each monomer is proprietary information. The copolymer has an average molecular weight of 50,000.[3]

## Chemical and/or Trade Names

Other names used to identify this cosmetic ingredient are listed below.[2,4]

Crotonic Acid, Polymer With Vinyl Acetate
2-Butenic Acid, Polymer With Ethenyl Acetate
Crotonic Acid-Vinyl Acetate Copolymer
Crotonic Acid-Vinyl Acetate Polymer
Vinyl Acetate-Crotonic Acid Polymer

## Properties

The major properties of VA/CA Copolymer are determined by its acid content, which can vary. An acid content of 3%–14% renders the copolymer soluble in slightly alkaline media.[5,6] Solubility of the polymer increases in polar solvents and decreases in nonpolar solvents as the number of crotonic acid units in the polymer increases. An increased acid content also increases the softening point but decreases the viscosity of solutions containing the polymer.[7]

VA/CA Copolymer is soluble in ethanol and 91% isopropanol. The polymer is not readily soluble in anhydrous isopropanol; however, complete solubility can be attained by the addition of minor amounts of methylene chloride. The copolymer is also soluble in aqueous bases, thus assuring its complete removability from skin and hair by soaps and shampoos.[1]

The melting point of VA/CA Copolymer varies from 85° to 145°C, the precise temperature depending upon acid content. The copolymer is also reported to be stable at 120°–140°C for short periods of time; however, when it is kept at 140°C for several minutes, a noticeable change occurs in the resin's infrared spectrum.[5]

In the formulation of cosmetic products, ethanol solutions of VA/CA Copolymer are neutralized with aminohydroxy compounds to form a resin that is both water and solvent soluble.[1,8] Thus, the copolymer exists in cosmetic formulations as the neutralized salt.[8] Several of the bases commonly used by cosmetic formulators to neutralize this ingredient are listed in Table 1. The amount of each base in grams required to neutralize 100 grams of VA/CA Copolymer is indicated; the degree of neutralization shown ranges from 70% to 100%.[1]

Film flexibility (resin hardness), hygroscopicity, and water solubility of VA/CA

**TABLE 1.** Grams of Base Required to Neutralize 100 G of VA/CA Copolymer.[a]

| Base used | Neutralization (%) | | | |
|---|---|---|---|---|
| | 70 | 80 | 90 | 100 |
| AMP (2-amino-2-methyl-1-propanol) | 7.238 | 8.272 | 9.306 | 10.340 |
| AEPD (2-amino-2-ethyl-1,3-propanediol) | 9.675 | 11.058 | 12.440 | 13.822 |
| THMAM (tris hydroxy methyl-amino methane) | 9.838 | 11.242 | 12.648 | 14.052 |
| $NH_3$ (28%) | 4.929 | 5.633 | 6.337 | 7.041 |
| MORPHOLINE | 7.072 | 8.085 | 9.095 | 10.105 |
| AMPD (2-amino-2-methyl-1,3-propanediol) | 8.525 | 9.745 | 10.962 | 12.180 |

[a]Data from Ref. 1.

Copolymer can be modified by varying the amount of the neutralizing agent. As the percentage of the polymer that is neutralized increases up to approximately 20%, resin hardness increases; at a neutralization greater than 20%, film hardness decreases. Film hardness may also be controlled by varying the type of neutralizing agent.[1]

Extended storage of formulations containing VA/CA Copolymer in lead soldered containers can result in some resin insolubilization. The use of tin solder has been suggested to insure maximum stability. Thus, VA/CA Copolymer beads can be stored without undergoing decomposition or degradation.[1]

The solubility and dissolution behavior of VA/CA Copolymer under a variety of experimental conditions has been studied by El-Khawas et al.[9] and El-Egakey et al.[10] These authors observed that dissolution of the copolymer is a function of its crotonic acid content and that it is influenced by the pH, ionic strength, and buffer concentration of the dissolution medium. The hygroscopicity and hardness of VA/CA Copolymer at varying humidities, as well as factors affecting the hydrolysis of the resin, have also been studied.[11,12]

El-Egakey et al.[5] reported that the UV absorption spectrum for VA/CA Copolymer is affected by the acid content of the resin and noted that it can vary from one batch to another. Ethanol solutions containing 0.5% and 5.0% VA/CA Copolymer have also been shown to absorb light minimally in the UV-B range of 280–320 nm.[13] Table 2 lists additional properties of VA/CA Copolymer.

**TABLE 2.** Chemical and Physical Properties.

| | | Ref. |
|---|---|---|
| Appearance | Fine, transparent beads | 1 |
| Volatile (%) | 2.0 maximum | 3 |
| Acidity | 1.10–1.24 meq/g | 1,3 |
| Specific gravity | 1.202 (23°C/23°C) | 1 |
| Intrinsic viscosity | 0.3 (in acetone at 30°C) | 1 |
| Water solubility: | | 1 |
| at ≤ 50% neutralization | poor | |
| at 70% neutralization | fair | |
| at 80% neutralization | good | |
| at ≥ 90% neutralization | excellent | |

## Analytical Methods

VA/CA Copolymer may be determined by infrared and ultraviolet spectroscopy.[5]

## Methods of Manufacture and Impurities

VA/CA Copolymer is manufactured by polymerization of vinyl acetate and crotonic acid monomers. A nonaromatic, nonazo, "peroxide-type" free radical is used as an initiator. Following polymerization, calcium stearate is added to help maintain the free-flowing properties of the resin. Water is subsequently added, and the mixture is steam distilled to remove unreacted monomer. The polymer is then water washed, filtered, and dried.[3] Calcium stearate is removed by filtration following formulation of the cosmetic product but prior to filling of the product container.[8]

A similar method described by Lundell et al.[14] involves polymerization of vinyl acetate and crotonic acid under aqueous emulsion conditions at 65° to 69°C using potassium persulfate as initiator. Small amounts of sodium acetate are added as a buffer for the crotonic acid. At low crotonic acid content (8%), the reaction is slightly exothermic; whereas, with crotonic acid levels greater than 10%, the reaction is more "sluggish." The authors reported that high molecular weights of VA/CA Copolymer are unobtainable because of the chain transfer activity of crotonic acid.

Johanson[7] described a method in which vinyl acetate and crotonic acid are combined at 70°C using benzoyl peroxide $(C_6H_5CO)_2O_2$ as initiator. This procedure yields products containing from 5.5% to 43% crotonic units.

Impurities in the raw material sold for commercial use include vinyl acetate ($CH_3COOCH=CH_2$), crotonic acid ($CH_3CH=CHCOOH$), and calcium stearate $Ca[OOC\text{-}(CH_2)_{16}CH_3]_2$. Total residual monomers are reported to be 500 ppm maximum, whereas calcium stearate is present in the finished dry product at approximately 0.01%.[3] The chemistry and biology of both vinyl acetate and calcium stearate have been reviewed elsewhere.[15-17]

# USE

## Purpose and Extent of Use in Cosmetics

VA/CA Copolymer is primarily used as a film forming agent in aerosol hair sprays and other hair preparations.[1] The resin helps to preserve the curl and shape of the hair after styling.[18]

Since VA/CA Copolymer is primarily used in hair preparations, it is likely to come in contact with the hair, scalp, face, neck, hands, and the fingernails. It may also come in contact with the eyes and respiratory tract.

Product formulations containing VA/CA Copolymer may be used from once a week to several times a day. Many of the products could remain in contact with the skin and hair for as briefly as one day to as long as several days. Each product has the possibility of being applied hundreds of times over the course of several years.

Product types and the number of product formulations voluntarily reported to the Food and Drug Administration (FDA) in 1976 as containing VA/CA Copolymer are listed in Table 3. Voluntary filing of such information by cosmetic manufacturers and formulators conforms to the prescribed format of preset concentration ranges and product types as described in the Code of Federal Regulations (21 CFR 720.4). In 1976, VA/CA Copolymer was reported as an ingredient in 55 cosmetic formulations at concentrations ranging from approximately 0.1%–25%.[19] Table 3 also lists FDA product formulation data for 1979. As noted, VA/CA Copolymer was reported as an ingredient in a total of 90 formulations. Thirty-six formulations contained the ingredient at levels of about 0.1%–10%; whereas, the concentration level was not reported in 54 of the products. Data on product categories were unavailable for 1979.

It is important to note that the type of data found in Table 3 has certain limitations. Since certain cosmetic ingredients are supplied by the manufacturer at less than 100% concentration, the value reported by the cosmetic formulator or manufacturer may not necessarily reflect the true, effective concentration found in the finished product; the effective concentration in such a case would be a fraction of that reported to the FDA. The fact that data are only submitted within the framework of preset concentration ranges also provides the opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end of that range, thus introducing the possibility of a two- to tenfold error in the assumed ingredient concentration.

## Potential Interactions with Other Cosmetic Materials

Solutions of neutralized VA/CA Copolymer in anhydrous SD Alcohol-40* are compatible with certain grades of shellac, whereas 82% neutralized VA/CA Copolymer is compatible with various animal proteins. Plasticizers such as cetyl alcohol, oleyl alcohol, butyl phthalyl butyl glycolate, and dimethyl phthalate are also reported to be compatible in all proportions with VA/CA Copolymer solutions.[1]

## Vehicles in Which Commonly Used

In aerosol hair sprays, anhydrous ethanol and 91% isopropanol are used as vehicles for VA/CA Copolymer.[1]

## Noncosmetic Use

VA/CA Copolymer is used as a dry binder for drug tablets[22-4] and as a coating or as a component of a coating for polyolefin films intended for packaging bakery products and confectionery (21 CFR 175.350). Because of its thromboresistant properties, the 60% sodium inomer of vinyl acetate/2% crotonic acid has been suggested for use in polyelectrolyte hydrogel coatings for biomedical applications.[25]

*SD Alcohol 40 (CTFA Name) is ethyl alcohol denatured in accordance with 27 CFR 212.57.

**TABLE 3.** Product Formulation Data.[a]

| Product category[b] | Total no. containing ingredient | No. product formulations within each concentration range (%)[b] | | | | | |
|---|---|---|---|---|---|---|---|
| | | Unreported concentration | >10–25 | >5–10 | >1–5 | >0.1–1 | ≤0.1 |
| Hair conditioners | 4 | – | – | 3 | 1 | – | – |
| Hair sprays (aerosol fixatives) | 30 | – | 1 | – | 27 | 2 | – |
| Tonics, dressings, and other hair grooming aids | 2 | – | – | – | 2 | – | – |
| Wave sets | 9 | – | – | – | 9 | – | – |
| Other hair preparations (noncoloring) | 10 | – | – | 1 | 9 | – | – |
| 1976 TOTAL ALL PRODUCTS | 55 | – | 1 | 4 | 48 | 2 | – |
| 1979 TOTAL ALL PRODUCTS[c] | 90 | 54 | – | 1 | 33 | 2 | – |

[a]Data from Ref. 19.

[b]Preset product categories and concentration ranges in accordance with federal filing regulations (21 CFR 720.4).

[c]Data from Ref. 20 and 21.

## BIOLOGICAL PROPERTIES

### Hematological Studies

In vivo and in vitro blood compatibility studies established that the 60% sodium ionomer of vinyl acetate/2% crotonic acid was the most antithrombogenic material in a series of polymers and ionomers.[14,25-7] The antithrombogenic activity of carboxyl containing copolymers such as VA/CA Copolymer depends upon the interaction between several physical and chemical parameters, including the total concentration of ionizable groups, the degree to which the copolymer is neutralized to various monovalent or divalent metal salts, and the hydrophilicity of the total polymer system.[14]

### Animal Toxicology

#### Acute Toxicity

*Oral*

Three groups of Holtzman rats (ten animals per group) were each given a single oral dose of an aqueous solution containing 3.7% VA/CA Copolymer neutralized with 0.4% 2-amino-2-methyl-1,3-propanediol. The test material was administered intragastrically to each group at levels of either 25, 37.5, or 50 ml/kg. No deaths occurred during the seven-day observation period following administration; the animals ate well and showed no visible toxic effects. All of the animals showed a normal weight gain.[28] Since the LD50 of the aqueous VA/CA Copolymer solution was >50 ml/kg, the LD50 of the ingredient can be calculated to be >1.85 ml/kg. On the basis of these results, the test material is classified as "relatively harmless," and the ingredient is, at most, "slightly toxic."[29]

A hair spray containing 13.75% VA/CA Copolymer was tested for acute oral toxicity in ten rats by means of the protocols stipulated in the Federal Hazardous Substances Act (FHSA) (16 CFR 1500.3). No mortalities or toxic signs were noted following administration of a single 5 g/kg dose of the product.[30]

*Skin Irritation*

The Draize method[31] was used to test the skin irritating ability of an aqueous solution containing 3.7% VA/CA Copolymer neutralized with 0.4% 2-amino-2-methyl-1,3-propanediol. The test material (0.5 ml) was applied to the intact and abraded skin of each of three albino rabbits. Test sites were evaluated at the end of 24 and 72 hours. None of the animals demonstrated irritation.[28]

A hair spray containing 13.75% VA/CA Copolymer was tested for dermal irritation by means of the procedures described in the FHSA (16 CFR 1500.41). The test material was applied under an occlusive patch to the intact and abraded skin of each of six albino rabbits. After 24 hours of exposure, the patches were removed and the test sites graded; evaluations were repeated 48 hours following the initial reading. No irritation was observed in any of the animals.[30]

*Eye Irritation*

An aqueous solution containing 3.7% VA/CA Copolymer neutralized with 0.4% 2-amino-2-methyl-1,3-propanediol was tested for eye irritation by means of the Draize method.[31] The test material (0.1 ml) was instilled into the right eye of each of three albino rabbits; the left eye of each animal served as control. The treated eyes remained unwashed. Eyes were examined for irritation every 24 hours for four days and then again on the seventh day. Conjunctival irritation was observed in each of the rabbits on days 1–4, but not on day 7. Average scores* were 4.7, 4.0, 2.0, 2.0, and 0.0 on days 1, 2, 3, 4, and 7, respectively, indicating that the test material is a minimal eye irritant.[28]

The eye irritation potential of a hair spray containing 13.75% of the copolymer was determined in six albino rabbits using the protocols stipulated in the FHSA (16 CFR 1500.42). Each animal had 0.1 ml of the test material instilled into one eye with no further treatment; the untreated eye served as control. Slight conjunctival irritation and discharge were observed for two days following instillation of the test material; however, the treated eyes appeared clear by day 3.[30]

## Subchronic Inhalation Toxicity

Three aerosol spray formulations designated as A, B, and C were tested in a 90-day subchronic inhalation study. Formulation A had the following composition:

| | *Percent* |
|---|---|
| VA/CA Copolymer | 0.86 |
| AMPD (2-amino-2-methyl-1,3-propanediol) | 0.08 |
| Wool fat, ethoxylated | 0.036 |

*Max. score possible per animal per observation = 110.

| | |
|---|---|
| Silicone oil | 0.036 |
| Perfume | 0.061 |
| Ethanol | 34.927 |
| Propellant: trichloromonofluoromethane and difluorodichloromethane | 64.00 |
| | 100.00 |

Formulation B was of the same composition as A, except that the perfume was omitted and the difference made up with additional alcohol. Formulation C was a commercial hair spray of similar composition except that no VA/CA Copolymer was used in its formulation. The experimental procedure was that of Draize et al.[32] Each of the three formulations was administered by means of a 30-second aerosol burst into a chamber housing six (3M, 3F) New Zealand rabbits. A fourth group of six animals served as untreated control. Following exposure, animals remained in the resulting atmosphere of the closed chamber for 15 minutes. Aerosol exposures were given twice a day for five consecutive days every week of the 90-day study for a total of 67 exposure days and 134 exposures. Throughout this period, mean body weights and total weight gains of the treated animals remained normal. No untoward behavioral reactions or abnormalities with respect to blood hemoglobin concentration, erythrocyte count, and total and differential leucocyte counts were observed in any of the treated animals as compared to controls. Anterior-posterior radiographs of lungs at the conclusion of the study revealed no indication of exposure-related abnormalities. The results of gross and histopathologic studies of the liver, spleen, kidney, bone marrow, cervical and thoracic lymph nodes, thymus, lungs, and trachea were "essentially negative" for all groups tested.[33]

### Mutagenesis

Although no mutagenic data are available on VA/CA Copolymer, there are data on the vinyl acetate portion of the copolymer.

Exposure of *Salmonella typhimurium* TA100 and TA1530 to vapors of vinyl acetate in the presence or absence of a 9000 × g supernatant fraction of liver from phenobarbital-pretreated mice caused no mutagenic effects.[15,16,34-6]

No mutagenic effects were detectable in *Salmonella typhimurium* strains TA100, TA98, TA1535, or TA1537 when the organisms were exposed in vitro to vinyl acetate with and without the addition of S-9 rat liver metabolic activation preparation. The liver preparation was taken from rats treated with Aroclor 1254. The number of revertants/nmol of the exposed bacteria were $<0.0006$; levels of $<0.01$ revertants/nmol were considered nonmutagenic.[37]

### Carcinogenesis

No carcinogenesis test data are available on VA/CA Copolymer; however, test data on the vinyl acetate portion of the copolymer are available from a number of studies conducted to evaluate the carcinogenesis of vinyl chloride. In several of these studies, vinyl acetate was tested for comparative purposes. A group of 96 Sprague-Dawley rats (sex not specified) was exposed for four hours

per day, five days per week for 52 weeks to the maximum tolerated concentration of 8.8 g/m$^3$ (2500 ppm) vinyl acetate in air. No tumors were reported to have occurred during 135 weeks. Early mortality was high with only 49 animals surviving 26 or more weeks.[15,16,38-41] The time of death of animals that lived longer than 26 weeks was not reported. No indication that crotonic acid has been studied for carcinogenesis or cocarcinogenesis has been found.

## Clinical Assessment of Safety

### Skin Irritation and Sensitization

The Shelanski Repeated Insult Patch Test Method[42] was used to evaluate the skin irritation and sensitization ability of a hair spray containing 0.86% VA/CA Copolymer, 0.08% AMPD, 35.06% ethanol, and 64% propellant. The test material was sprayed directly onto a lintine disc which was then placed in contact with the skin of each of 50 subjects (25M, 25F). The amount of spray required to saturate the disc was approximately 500 mg, and the area of skin contact was approximately one square inch in size. Following a 24-hour exposure, the disc was removed and the skin left uncovered for 24 hours. This procedure was repeated 15 times over a 30-day period. A 48-hour challenge disc containing the test material was applied two to three weeks after the fifteenth induction application. No signs of irritation or sensitization were observed in any subject.[43]

In a second study, an aerosol hair spray containing 0.86% VA/CA Copolymer, 0.08% AMPD, 35.06% ethanol, and 64% propellant was tested for skin irritation and sensitization according to the methods of Shelanski and Shelanski.[42] The formulation was sprayed through a cone onto the skin of each of 50 women, and each test site was covered with a patch. Approximately 500 mg of spray was required to wet one square inch of skin. Following a 24-hour exposure, the patches were removed, and the skin was left uncovered for 24 hours. This procedure was repeated 15 times over 30 days. Two to three weeks after the fifteenth induction application, the test material was reapplied under a patch for 48 hours. None of the subjects showed skin irritation or sensitization.[44]

### Inhalation

Twenty-five women, four with a history of "some allergic manifestation," used a hair spray containing 0.86% VA/CA Copolymer together with solvents, perfumes, and propellants. Exposure was designed to be of the type encountered in customary hair grooming. One 14-oz. can of hair spray was used each month over a period of one year, a consumption rate reported to be significantly greater than that of the "average user of hair spray." Each woman received a "thorough" medical history and physical examination, including a complete blood count, urinalysis, chest X ray, and electrocardiogram at the outset of the study, after six months, and after one year. Despite the high proportion (4/25) of subjects with an allergic diathesis, none of the women showed any toxicologic effect.[45]

Three hair spray preparations were studied by Zuskin and Bouhuys[46] for their acute airway response. Sixteen human subjects inhaled on alternate days a spray containing an unspecified concentration of VA/CA Copolymer, a second

spray formulation containing polyvinylpyrrolidone, and a placebo of water and nitrogen. Each spray was administered continuously and directed at the hair for 20 seconds while the subjects breathed normally. From recordings of maximum expiratory flow (MEF) curves, maximum flow rates at two volume levels were measured: (1) total lung capacity minus 50% of control vital capacity (MEF 50%), and (2) total lung capacity minus 75% of control vital capacity (MEF 25%). Values of MEF 50% and MEF 25% reflect maximum flow rates at a constant degree of lung inflation. Changes of MEF 50% and MEF 25% indicate changes in maximum expiratory flow rates at equal degrees of lung inflation. Test results showed that after spray exposure, flow rates on partial and maximum expiratory flow-volume curves were reduced. Three of the 16 subjects complained of chest tightness and difficulty in breathing throughout the experiment. The flow rates usually returned to control values within two or three minutes; however, ten minutes after exposure, a residual effect still existed. At 60 minutes post-exposure, partial expiratory flow-volume curves remained below normal in all subjects. At this latter point in time, MEF 50% and MEF 25% were decreased in three subjects. The placebo caused a slight but statistically significant reduction of the MEF 50% immediately after exposure; later measurements were slightly but not significantly larger than control values. At each point in time after exposure to hair spray, flow rates differed significantly from the comparable measurements following placebo aerosol. These changes suggest that hair spray causes acute, reversible narrowing of the small airways, but the mechanisms of action of hair sprays on human airways is not clear. According to the authors, a given ingredient (or ingredients) may have a direct effect on airway smooth muscle, or may cause lung tissue to release histamine, or both; a release of histamine could account for the slow disappearance of the airway constrictor effect.

### Thesaurosis and Epidemiologic Studies

VA/CA Copolymer is one of several resins used in hair spray formulations.[8] Whether these hair spray polymers cause a unique lung disease known as "thesaurosis" is a matter of dispute.[47] Originally described by Bergmann et al.[48], thesaurosis is a disorder reported to be caused by the pulmonary accumulation and storage of hair spray resins. Between 1958 and 1973, 30 cases of alleged thesaurosis were published in the literature; however, the preponderance of evidence in the literature to date does not support an etiologic relationship. Many investigators have argued that various pulmonary disorders (sarcoidosis and other granulomatoses) following exposure to polymer inhalants are coincidental and nonspecific in character. Discher and Hall[47] have reviewed the literature on the thesaurosis controversy.

Palmer et al.[49] conducted an epidemiologic survey of respiratory disease prevalence in cosmetologists and found a higher prevalence of chest X-ray indicators of thesaurosis in employees of beauty salons as compared to control subjects and cosmetology students. Twenty-five of 475 cosmetologists and 21 of 569 noncosmetology control subjects demonstrated one or more of three abnormalities (abnormal chest X ray, reduction of forced vital capacity, or diffusion capacity of the lung) that suggested the presence of thesaurosis. As a result of a two-year followup study designed to validate this survey, Renzetti et al.[50] found

that "Neither the chest x-ray findings nor the results of pulmonary function testing substantiate the concept that there is such a disease as thesaurosis from hair spray exposure."

Discher and Hall[47] reported the results of an epidemiologic study that assessed the cardiorespiratory health status of 933 cosmetologists occupationally exposed to aerosolized hair sprays. No clinically significant differences were observed between the cosmetologists and a similarly sized control group of women telephone workers with respect to pulmonary function tests, electrocardiography, chest X ray, or sputum cytology.

### Estimated User Exposure to Respirable Particles

Mokler[51] described the results of a study designed to characterize the respirable particles generated during the use of aerosolized hair sprays. Variations in use conditions and techniques appeared to have little effect on particle size characteristics and only a "modest" effect on aerosol concentration. Four aerosol hair sprays were each directed onto a wig with atmospheric sampling being done in the area of the wig holder representing placement of the mouth. Distance from the aerosol source to the target was 15 cm. Air sampling for 12 seconds during and 48 seconds following gave breathing zone concentrations ranging from 18 to 62 mg/m$^3$ for the four samples. According to CTFA,[8] this exposure can be calculated to be 30 times less than allowed by the Occupational Safety and Health Administration (OSHA) for a respirable nuisance dust.

The American Conference of Government Industrial Hygienists[52] reports that the Threshold Limit Value–Time Weighted Average (TLV–TWA) of vinyl acetate is 10 ppm or 30 mg/m$^3$. The TLV–TWA is defined as "the time-weighted average concentration for a normal 8-hour workday or 40-hour workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect." The Threshold Limit Value–Short Term Exposure Limit (TLV–STEL) of vinyl acetate is reported to be 20 ppm or 60 mg/m$^3$. The TLV–STEL is defined as the maximum concentration to which workers can be exposed during any 15-minute period without adverse effect, provided that no more than four excursions per day occur, with at least 60 minutes between exposures, and provided that the daily TLV–TWA is not exceeded. Threshold limit values refer to airborne concentrations of substances.

The National Institute for Occupational Safety and Health[15] recommends that exposure to vinyl acetate in the workplace be controlled so that employees are not exposed to concentrations greater than 15 mg/m$^3$ (4 ppm), measured as a ceiling concentration in samples collected during any 15-minute period.

## DISCUSSION

The animal and human toxicity tests on VA/CA Copolymer and on cosmetic products containing the ingredient, as presented here, are rather limited. The results reported, however, are sufficient to show the safety of single exposures to this ingredient with respect to oral toxicity, and skin and eye irritation, and of repeated exposures with respect to skin irritation and sensitization. It should be

noted that all repeated insult patch tests for skin irritation and sensitization in the human were done with hair spray formulations containing only 0.86% VA/CA Copolymer. In evaluating these studies, however, one has to consider the actual concentration of the copolymer on the skin after evaporation of carrier (usually ethanol) and the hair spray propellants. Since ethanol and propellant comprised approximately 99% of the product, and since about 500 mg of the formulation contacted the skin following spray application, one can predict that the final VA/CA Copolymer concentration on the skin is much higher than 0.86%, and therefore sufficient for an evaluation of safety.

Although there were no human or animal test data available on phototoxicity and photoallergenicity, physical data were available. These data indicated that ethanol solutions containing 0.5% or 5.0% of the copolymer minimally absorb light in the UV-B range of 290–320 nm. For a nontoxic compound to induce a photosensitive response, it is generally agreed that some structural change must occur in the test material following light exposure. While absence of absorption in the UV range of 280–400 nm ensures that a photosensitivity potential does not exist, the converse is not true. Absorption only indicates an energy capture phenomenon and does not mean that any change induced will create a photosensitizing configuration. Although the Panel prefers actual clinical or animal test data, the failure of the VA/CA Copolymer-ethanol solution to significantly absorb UV light was considered sufficient to demonstrate a low risk for photosensitization.

All the data thus far reported for both animals and humans to assess the inhalation toxicity of VA/CA Copolymer were derived from formulation studies in which the concentration of the ingredient was only 0.86%. In these inhalation tests, the whole aerosol, including propellant, is inhaled, and the effective exposure concentration of the ingredient is assumed to remain at 0.86%. This is significantly below the concentration present in some of the formulations. Epidemiologic surveys of cosmetologists, however, who have worked with products containing higher concentrations of the VA/CA Copolymer, have not revealed evidence of adverse effects on the health status of these workers. It can thus be concluded that the health of the general consumer, whose exposure is much less than that of the cosmetologist, would not be adversely affected.

## SUMMARY

Vinyl Acetate/Crotonic Acid Copolymer is a polymer formed from vinyl acetate and crotonic acid monomers. In the formulation of cosmetic products, ethanol solutions of VA/CA Copolymer are neutralized with aminohydroxy compounds to form a resin which is both water and solvent soluble. Thus, the copolymer exists in cosmetics as the neutralized salt. Although morpholine may be used in the preparation of this ingredient, safety assessment did not include this compound. Impurities in the material sold for commercial use include vinyl acetate, crotonic acid, and calcium stearate.

VA/CA Copolymer is primarily used as a film forming agent in aerosol hair sprays and other hair preparations. Cosmetic manufacturers voluntarily reported to FDA in 1979 that VA/CA Copolymer was an ingredient in 90 cosmetic products

at concentrations ranging from about 0.1% to 10%. Neutralized solutions of the copolymer are compatible with various animal proteins, plasticizers, and certain grades of shellac. The major uses of the resin are in hair preparations; thus, this ingredient may come in contact with the hair, scalp, face, neck, hands, fingernails, eyes, and the respiratory tract.

An aqueous solution containing 3.7% VA/CA Copolymer and a hair spray containing 13.75% of the ingredient were relatively harmless when administered to rats in single oral doses of up to 50 ml/kg and 5 g/kg, respectively. These same test materials elicited no skin irritation in rabbits and minimal, transient eye irritation.

In a subchronic inhalation study, rabbits exposed for 90 days to aerosolized formulations containing 0.86% VA/CA Copolymer showed no significant differences from controls with respect to mean body weights, total weight gain, behavior, blood hemoglobin concentration, erythrocyte count, total and differential leucocyte count, radiographs of lungs, or gross pathology and histopathology. No mutagenic effects were detectable in *Salmonella typhimurium* when the organisms were exposed in vitro to vinyl acetate with and without the addition of S-9 rat metabolic activation preparations. No tumors occurred in rats exposed 52 weeks to 2500 ppm vinyl acetate in air.

Hair spray formulations containing 0.86% of the copolymer caused no skin irritation or sensitization when tested in repeated insult patch tests on humans. Taking into account the evaporation of propellants and ethanol from these products upon spraying, one can predict that the actual concentration of VA/CA Copolymer applied to the skin in these studies is much greater than 0.86%. No evidence of any toxicologic effect was observed in 25 women who for one year had used hair sprays containing 0.86% VA/CA Copolymer. One study demonstrated that hair spray preparations containing the polymer caused acute, reversible narrowing of airways in humans.

VA/CA Copolymer and other hair spray resins have been implicated by some investigators as the causal agent of "thesaurosis"; however, other investigators have argued that various pulmonary disorders of hair spray users are coincidental to hair spray exposure and are actually nonspecific in character. Recent epidemiologic surveys of respiratory disease prevalence have demonstrated no significant differences between cosmetologists occupationally exposed to hair spray inhalants and nonexposed control subjects with respect to chest X rays, pulmonary function tests, sputum cytology, or electrocardiographs.

## CONCLUSION

On the basis of the available information presented in this report, the Panel concludes that Vinyl Acetate/Crotonic Acid Copolymer is safe as a cosmetic ingredient under present practices of product and concentration use.

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