File No: NA/708

January 2001

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

AVC-10

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Director
Chemicals Notification and Assessment

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1. APPLICANT

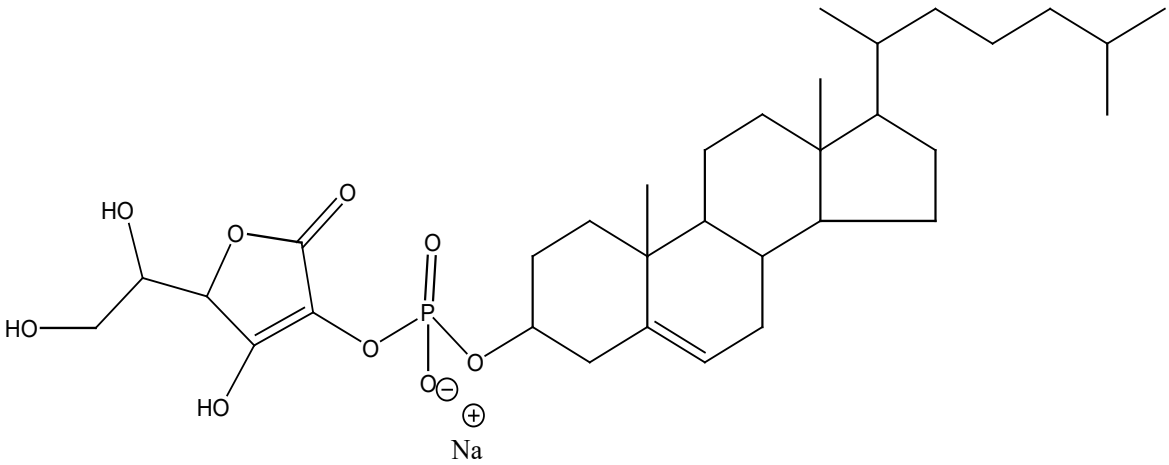
Avon Products Pty Ltd of 120 Old Pittwater Road BROOKVALE NSW 2100 (ACN 008 428 457) has submitted a limited notification statement in support of their application for an assessment certificate for AVC-10.

The notifier has not requested any information relating to the notified chemical to be exempt from publication in the Full Public Report and Summary Report.

2. IDENTITY OF THE CHEMICAL

Chemical Name:	L-ascorbic acid, 2-[(3)-cholest-5-en-3-yl hydrogen phosphate], monosodium salt
Chemical Abstracts Service (CAS) Registry No.:	185018-43-3
Other Names:	Sodium ascorbyl/cholesteryl phosphate
Marketing Name:	AVC-10
Molecular Formula:	$C_{33}H_{52}O_9NaP$

Structural Formula:



Molecular Weight:	646.7

Method of Detection and Determination:	Infrared (IR) spectrum
Spectral Data:	IR spectrum peaks are 3328, 2935, 1731, 1592, 1465, 1380, 1228, 1040, 960, 899, 806, 734, 683 and 550 cm^{-1}

Comments on Chemical Properties

An IR spectrum has been provided for the identification of the chemical.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance:	White to off white powder
Melting Point:	150°C
Specific Gravity:	Not determined (see comments below)
Vapour Pressure:	Not determined (see comments below)
Water Solubility:	150 g/L at 20°C
Partition Co-efficient (n-octanol/water):	Not determined (see comments below)
Hydrolysis as a Function of pH:	Not determined (see comments below)
Adsorption/Desorption:	Not determined (see comments below)
Dissociation Constant:	Not determined (see comments below)
Particle Size distribution:	2.3μm: <10% 4.8μm: <25% Average: 10 – 15 μm
Flash Point:	Not determined (see comments below)
Flammability Limits:	Not flammable
Autoignition Temperature:	Not determined; 500 - 600°C based on components
Explosive Properties:	Not explosive
Reactivity/Stability:	Incompatible with combustion agents, oxidising agents and alkalis

Comments on Physico-Chemical Properties

The test methods used cannot be confirmed; however, the notifier claims that the water solubility test was conducted according to OECD TG 105. The full test report for water solubility was not provided. The notifier has indicated that R&D Analytical Department, Avon Products, Inc., conducted the water solubility test using a 15% w/w aqueous solution method at 20°C. The material is a salt and contains a polar ascorbyl group, as well as a hydrophobic cholesteryl functional group. The polar group is likely to increase the water solubility of the chemical, but the cholesteryl group will be fat-soluble. However, the combined effect is unclear and without detailed tests or other information the claimed high solubility (150 g/L) cannot be confirmed.

The notifier indicated that there is limited information on hydrolysis and dissociation constant for the notified chemical. The chemical exhibited some dissociation; however, the partition coefficient could not be determined.

The notifier provided information on the hydrolysis and dissociation constant for the product process quality assurance. This information cannot be used in the environmental hazard assessment for the notified chemical. The hydrolysis was tested using bicarbonate solution at room temperature for an "intermediate" (acetomide), which is limited to a maximum of 2% hydrolysis. This result suggests that hydrolysis in weak base does not occur readily. However, under appropriate conditions it is likely that this chemical will hydrolyse in the environment.

Due to its bipolar structure, the chemical may be surface active and may bind to organic material and other surfaces in the environment. Since the chemical is a phosphate salt, it is already fully dissociated.

The physico-chemical properties of the notified chemical such as boiling point, water solubility, partition coefficient, hydrolysis and biodegradability, cannot be determined using the USEPA ASTER Estimation Model because of its chemical structure.

4. PURITY OF THE CHEMICAL

Degree of Purity: >99%

Hazardous Impurities: None known

Non-hazardous Impurities: Moisture and ash

Additives/Adjuvants: None known

5. USE, VOLUME AND FORMULATION

The notified chemical, AVC-10, will not be manufactured in Australia. It will be imported as a powder in 10.5 kg double lined containers at 300 kg per year for the next 5 years. The notified chemical will be formulated with other components in skin cosmetic products such as liquids, lotions or cream formulations. The final product will contain 2.5% notified chemical in consumer packs of up to 150 mL.

The skin conditioner product will be used by the general public.

6. OCCUPATIONAL EXPOSURE

The notified chemical will be imported in a powder form. It will be compounded with other ingredients to produce a cosmetic product containing 2.5% notified chemical. The finished cosmetic product will be packed in up to 150 mL consumer packs ready for retail distribution.

There will be 2 personnel involved in transport and storage of the notified chemical (2 hours per day, 4 days per year) following importation. These workers are not expected to be exposed to the chemical unless the packaging is breached.

Manufacturing of cosmetic products

Three (3) manufacturing sites will be producing cosmetic products containing the notified chemical. The following table describes the categories of workers with potential exposure to the notified chemical and the estimated exposure during manufacture:

Categories of workers	*Number of workers*	*Estimated exposure*
Chemical dispensers	3	2 hours per day, 4 days per year
Chemical compounders	6	2 hours per day, 4 days per year
Laboratory technicians	6	6 hours per day, 2 days per year
Packaging process operators	50	4 days per year

At the dispensary, chemical dispensers will weigh the requisite amount of chemical powder (>100%) and transfer it in sealed plastic bags contained in plastic buckets to the product manufacturing area.

At the manufacturing area, chemical compounders will add the pre-weighed chemical into a 1 200L cosmetic cream mixing tank through a top mounted manhole, where it is mixed with other ingredients. The mixing tank is heated to form emulsions of the final product. Each batch of cooled emulsion is pumped directly into 1 000L plastic bag contained in pallecons. These are sealed and transported to the filling area where they are connected to filling machinery dispensing into 150mL polyethylene containers.

The main exposure to the notified chemical occurs during weighing and feeding the mixing tank where skin contact and potential inhalation of chemical dusts may occur. The formulation and filling are carried out in an enclosed and automated system. Dermal exposure to spills and drips of the manufactured product containing the notified chemical at 2.5% is possible while connecting and disconnecting pumps during transfer of emulsions to plastic bags prior to transport to the filling area. Similarly, cleaning and maintenance of the equipment may involve dermal exposure to the diluted final product.

Chemical dispensers and compounders who will handle both the chemical powder and the diluted final product. Local exhaust ventilation is used during these processes and workers will wear personal protective equipment including gloves, safety glasses, hair covering and facemasks, if necessary. Filling and packaging operators who will only be exposed to the final consumer product will have access to similar personal protective equipment if needed.

Laboratory
Laboratory technicians prepare trial batches and test the quality of the final products. Exposure to both the powdered chemical and the diluted final product containing the notified chemical may occur; however, the quantities handled are small. Laboratory facilities such as fume hoods would be available. The laboratory staff will wear laboratory coats, gloves and safety glasses.

7. PUBLIC EXPOSURE

Cosmetic products containing the notified chemical will be sold to the public who will make dermal contact with the notified chemical. Dermal exposure of individual to varying amounts of products containing the notified chemical is likely to occur on a daily basis, with possible accidental ocular exposure also likely. The extent of public exposure to the notified chemical is dependent upon the extent of market penetration of products containing the notified chemical. Public exposure to the notified chemical from environmental sources is unlikely because release of the notified chemical is expected to be low and the notified chemical is likely to be biodegraded and present at low concentrations.

8. ENVIRONMENTAL EXPOSURE

Release
During reformulation, losses of the notified chemical will be attributed to spills, equipment washing and imported container residues. Since the notifier has not stated how much is lost due to spills or import container residue, it is estimated that both these sources may account for about 1% loss of notified chemical each (i.e. 3 kg due to spills and 3 kg in residues). No indication has been provided as to how the containers are treated or disposed of. It is therefore presumed that they are ultimately disposed of to landfill. This is also likely to be the case for any spilt powdered chemical.

The notifier has estimated that up to 10 kg of final product is left as residue in the reformulation equipment. The concentration of notified chemical in the final product is 2.5%, equivalent to 0.25 kg of waste notified chemical per batch. The size of a batch is 650L, and presuming this is equivalent to 650 kg, 1.5% of product is wasted. Therefore, annually 1.5% of the imported volume of notified chemical is disposed of in the resultant

wash water, which equates to 4.5 kg/year. The wash water at the Preston and Hornsby sites will be treated with flocculants to remove solids then undergo pH adjustment before being discharged to sewer.

Therefore a summary of the waste notified chemical generated during reformulation is:

spills – 1%	3 kg	likely disposed to landfill
import container residues – 1%	3 kg	likely disposed to landfill
equipment wash water – 1.5%	4.5 kg	likely disposed to sewer.

The notifier has not stated how much product remains in the "empty" end-use container. This assessment estimates that about 1% of product (37.5 mg of notified chemical) will remain in the "empty" end-use container. Since the general public uses this product, it is likely that the end-use containers will be disposed of in the domestic rubbish and will subsequently end up in a landfill. This would account for 75 g of notified chemical annually.

Once the product has been applied to skin any excess will be washed or wiped off, thus entering the sewer. No indication of retention by the skin has been provided, so it is presumed that all of the applied product will ultimately enter the sewer through skin washing, i.e. 95.5% (100% minus spills 1%, process equipment cleaning 1.5% and container residues 2%).

Fate

Ultimately all of the imported chemical will reach the environment, approximately 97.0% (95.5% plus 1.5%) via the sewer and the remainder (3%) via disposal to landfill.

Due to the chemical's possible surface activity, it may adsorb onto soil, sludge or sediment, and therefore be unlikely to leach from landfill. The chemical is likely to be used in small amounts across Australia, therefore should any chemical leach from landfill; it will be in a diffuse manner at very low levels.

The chemical is likely to undergo natural biodegradation, under both aerobic and anaerobic conditions, resulting in the release of oxygen, hydrogen, carbon in various forms, and sodium and phosphate ion. Other likely degradation products are ascorbic acid and cholesterol, both of which already occur in significant quantities in sewage effluent from domestic and industrial premises. However, the rate at which this may occur is unclear.

9. EVALUATION OF TOXICOLOGICAL DATA

The notifier provided a number of studies on the notified chemical or products containing the notified chemical, and analogue chemicals in support of the application. Summary reports on acute oral toxicity, skin irritation, eye irritation, skin sensitisation and photosensitisation and full reports on phototoxicity and genotoxicity were submitted. All data provided are evaluated as described below.

9.1 Metabolism

The notifier stated that the notified chemical AVC-10 consists of ascorbic acid (vitamin C) and cholesterol, linked through a phosphate group by ester bonds. Both ascorbic acid and

cholesterol are well-characterised and common ingredients in human diets and may reasonably be expected to be safe. Evidence was provided that *in vitro* incubation of human fibroblasts with AVC-10 over a period of 25 hours indicates that the substance undergoes a simple bioconversion to ascorbic acid and cholesterol (Tojo and Lee, 1987).

9.2 Acute Toxicity

9.2.1 Oral Toxicity

Notified chemical:
An acute oral toxicity study in a suitable animal model was not provided. The notifier stated that AVC-10, by virtue of its breakdown metabolites ascorbic acid and cholesterol, (Tojo and Lee, 1987), should be considered safe with respect to its acute oral toxicity. It is claimed that human poisonings with ascorbic acid are unknown (Clinical Toxicology of Commercial Products. 5th Ed. Baltimore: Williams and Wilkins, 1984, p266), with a probable human oral lethal dose in excess of 15 mg/kg. Animal data for ascorbic acid indicate an oral LD50 of 11.9 g/kg in the rat (Yakuri, 1976) and approximately 3 400 mg/kg in the mouse (National Cancer Institute Screening Program Data Summary, Developmental Therapeutics Program, January 1986). The second component, cholesterol, is a ubiquitous metabolite.

Analogue chemicals:
Support for the low oral toxicity of AVC-10 is provided by the analogue potassium salt of the ascorbyl tocopheryl phosphodiester, which has a rat oral LD50 > 4000 mg/kg (Senju Pharmaceutical Co., Ltd., Osaka, Japan). Further, magnesium ascorbyl phosphate, another phosphorylated ascorbic acid analogue, has a rat oral LD50 > 10 000 mg/kg (Barnet Products Corp., NJ, USA).

9.2.2 Acute Inhalation Toxicity

No data were submitted.

9.2.3 Skin Irritation

Notified chemical:
The notifier stated that AVC-10 is not a primary irritant and is considered to have negligible irritancy potential on human skin. The Primary Irritation Index (PII) was 0.08 (maximum = 4.0) in a human 24-hour occlusion test (Clinical Evaluation Report: Human Patch Test. Avon Products, Inc., Study No. APTC-1112-97, 1997). AVC-10 powder was applied to the skin of 19 subjects at a dose of 40 mg (10 mg/cm^2) via water saturated occlusive patches. In the same test, ascorbic acid demonstrated a PII of 0.21, and cholesterol had a PII of 0.11. Titanium dioxide and 0.05% sodium lauryl sulfate (aqueous) demonstrated PIIs of 0.03 and 1.3, respectively.

AVC –10 was also tested for skin corrosivity in the *Corrositex* Continuous Time Monitor Assay (Corrositex Continuous Time Monitor Assay, 1996), an *in vitro* method developed in response to UN Guidelines. This method is applicable to a limited number of materials including organic acids and acid derivatives such as the notified chemical and is accepted by several competent authorities including US DOT, OSHA, and EPA. All results were negative (i.e., non-corrosive) but in the absence of appropriate validation data, their significance cannot be determined.

A desquamation test was provided by the notifier; however the data were of insufficient quality for proper evaluation.

Preparation containing the notified chemical:
Cosmetic preparations containing AVC-10 at concentrations of 2.5% and 5% demonstrated negligible skin irritation potential when evaluated in human subjects (Clinical Evaluation Report, 1997a;b). Even under exaggerated occlusive exposure conditions of the 24-hour single insult patch tests, cosmetic lotions containing AVC-10 were essentially non-irritating (PII) = 0.03 and 0.08 at 2.5% and 5%, respectively).

9.2.4 Eye Irritation

Notified chemical:
The notifier stated that AVC-10 would only be considered to be a potential eye irritant by virtue of its physical form (powder). It was further stated that serious injury due to the chemical nature of AVC-10 is unlikely since the similar diester, EPC-K, is not a primary eye irritant in rabbits.

In vitro test data were provided with the EYTEX™ assay (EYETEX™ Assay, 1995), an alternate system to replace the Draize assay for predicting the eye irritation potential of raw materials, as well as oil/water emulsions. AVC-10 concentrations 1, 5, 10 and 20% were minimal eye irritants whereas undiluted AVC-10 appeared to be a moderate eye irritant. Data were also provided using the Chorioallantoic Membrane Vascular Assay (CAMVA-10 DAY), another alternative to the Draize assay for measuring eye irritation. Results indicated AVC-10 was non-irritating in this system.

The notifier claims that AVC-10 is not expected to pose an eye irritation hazard at typical usage concentrations intended for use in the eye area. This expectation is also supported by data from *in vitro* irritation assays, as well as long-term clinical tests and consumer use experience involving more than 400 subjects.

Five *in vitro* assays were conducted to evaluate the eye irritation potential of AVC-10 in product. Two EYTEX™ assays were run with AVC-10 at 2.5% and 5%, respectively, in cosmetic lotion with vehicles not identified (EYTEX™, 1996a;b). Both assays indicated only mild to moderate eye irritation. Recently, the EYTEX™ system was replaced by a modified version, the Irrifection assay (Irrifection Assay, 1996a,b), which has also been claimed to be predictive of Draize rabbit eye irritation. The same AVC-10 preparations were found to produce mild/moderate and moderate eye irritation, respectively, in the Irrifection assay. Finally, in a CAMVA10-DAY assay (Chorioallantoic Membrane Vascular Assay, 1995), a 2.5% lotion of AVC-10 was found to be non-irritating.

The notifier claims that AVC-10, at typical use concentrations in a cosmetic lotion vehicle, would be expected to produce nothing more than mild/moderate eye irritation. Further, in clinical use and consumer use tests lasting from 6 to 132 weeks and longer, AVC-10 at 2.5% in a cosmetic lotion did not produce any significant irritation.

9.2.5 Skin Sensitisation

Notified chemical:

The results from two human allergy studies indicate AVC-10 at 2.5% (n=25) and 5% (n=26) in cosmetic lotion vehicles (vehicles not identified) does not appear to possess any ability to induce skin sensitisation (Allergy Maximisation Test, 1997a;b), using the Kligman Maximisation procedure (details not provided). Test sites on the back were first treated with 0.5% sodium lauryl sulfate (SLS) under occlusive patches for 24 hours, followed by a 48-hour occlusive patch application of the test material. This 3-day cycle was repeated four times (total of 5 cycles). After a 10-day rest period, subjects were challenged at a naïve skin site treated for 1 hour with 10% SLS, followed again by a 48 hour occlusive patch application of test material. None of the subjects in either study exhibited a positive response to AVC-10 in cosmetic vehicle. Further, there was no evidence that AVC-10 (2.5% in cosmetic lotion) induced skin sensitisation as a result of repeated daily application in the long term clinical and consumer use tests (Clinical Safety In-Use (Face), 1996a,b,c, 1997; Consumer Use Test, 1997).

9.2.6 Photosensitisation

Notified chemical:
The notifier provided a summary of photosensitisation of the notified chemical.

AVC-10 at 2.5% in cosmetic vehicle had no detectable photocontact allergy potential when tested on human subjects (Photocontact Allergy Test, 1997). Test material was applied under occlusive conditions to the backs of 25 subjects and the application sites were irradiated 24 hours later with 3 MEDs (maximal erythemal doses) of UV light. This sequence was repeated two times per week for three consecutive weeks. Following a ten-to-fourteen day rest period, the material was applied to fresh skin sites under occlusion for 24 hours and then irradiated with 4 J/cm^2 of UVA radiations. Test sites were examined 48 and 72 hours after irradiation.

No side effects or unexpected reactions of any kind were observed. Following challenge, no reactions suggestive of photocontact allergy were seen in any of the subjects at either 48 or 72 hours post exposure.

9.2.7 Phototoxicity

Notified chemical:
AVC-10 demonstrated no phototoxic potential *in vitro* in the Yeast Phototoxicity Assay at concentrations of 0.1, 0.5, 1.0, 5.0 and 20% in water (Yeast Phototoxicity Test, 1995). No inhibition of growth was observed with any concentration of AVC-10 in the presence or absence of UVA irradiation.

9.3 Genotoxicity

The following tests were conducted using the notified chemical, AVC-10.

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (Wagner, 1996)

Strains:	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537, TA1538
Concentration range:	With and without S9: 100, 333, 1000, 3333, 5000 μg/plate

vehicle: water

Metabolic activation: 10% rat liver S9 fraction (Aroclor 1254-induced) in standard cofactors

Positive controls:

With S9:
All strains: 2-aminoanthracene, 1.0 μg/plate

Without S9:
TA98, TA1358: 2-nitrofluorene, 1.0 μg/plate
TA100, TA1535: sodium azide,1.0 μg/plate
TA1537: 9-aminoacridine, 75 μg/plate

Test method: Maron and Ames, 1983 (plate incorporation assay)

Comment: Precipitation was observed at ≥ 100 μg/plate without appreciable toxicity;

all test doses were plated in triplicate;

no significant increases in the frequency of revertants were recorded for any of the strains, at any dose level either with or without S9; all positive controls responded appropriately.

Result: The notified chemical was considered to be non-mutagenic under the conditions of the assay

9.3.2 Chromosome Aberrations in Chinese Hamster Ovary (CHO) Cells (Curry, 1996)

Cells: Chinese hamster ovary cells

Metabolic activation: rat liver S9 fraction (Aroclor 1254-induced) in standard cofactors

Experimental design: The assay was conducted in duplicate. The experimental design and concentrations tested are tabulated below.

Metabolic Activation	Test substance concentration (μg/mL)	Controls
-S9	20 hour harvest: 0, 15*, 29*, 57*, 113*, 168, 225, 337 and 450	Positive: 0.08μg/mL Mitomycin C Negative: Purified water

+S9	20 hour harvest: 0, 15, 29, 57*, 113*, 168*, 225*, 337 and 450	Positive: 10μg/mL cyclophosphamide Negative: Purified water

* cultures selected for metaphase analysis

Test method: Evans, 1976

Comment: in the presence and absence of S9, toxicity was observed at the highest test concentrations

positive and negative controls fulfilled the requirements for a valid assay

Result: the notified chemical was considered to be non-clastogenic under the conditions of the assay

9.4 Overall Assessment of Toxicological Data

Most of the data provided were of poor quality and employed a number of inadequately validated *in vitro* assays. In most cases, levels of detail provided were minimal or totally absent.

The notified chemical, AVC-10, is the sodium salt of a phosphodiester of ascorbic acid and cholesterol. These two components are common to plants and animals, are typically found in the human diet, and play key roles in several biological functions. An article was provided by the notifier to support the contention that AVC-10 is metabolised to its constituent components by esterases commonly found in animal and human tissues.

Acute oral toxicity values for the components were obtained from the literature and confirm that they have very low acute oral toxicity in rats. No study was available on the neat chemical. Analogue data indicated no adverse effects based on the end points examined in each of the tests systems.

Skin irritation studies were conducted in humans and in the *Corrositex* Continuous Monitor Assay *in vitro*. The data suggest that AVC-10 is a minimal skin irritant.

Eye irritation studies at various concentrations were performed using the EYTEX™ *in vitro* assay, a modified Irritection™ assay, and the Chorioallantoic Membrane Vascular Assay, test systems reported to have a high correlation with the standard Draize test. Data suggest that AVC-10 is a moderate eye irritant at 100% and a mild to moderate irritant at typical use in cosmetic lotion vehicles. The data were insufficient to determine a health effects classification.

Skin sensitisation potential of AVC-10 was evaluated in human volunteers. At 2.5% and 5% notified chemical in cosmetic lotion vehicles, there was no evidence of a positive reaction when tested using the Kligman Maximisation procedure. No photosensitisation reactions were seen in human subjects following challenge after an appropriate induction phase, nor was there any evidence of phototoxicity in the *in vitro* Yeast Phototoxicity Assay.

No repeat dose studies were submitted for evaluation.

AVC-10 did not show evidence of mutagenicity in bacteria or clastogenicity in mammalian cells *in vitro*.

Hazard classification

According to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999), the notified chemical cannot be classified as hazardous.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

No ecotoxicological data were provided.

ASTER Estimation Model calculations cannot be obtained for the notified chemical since the chemical structure is unsuitable.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

Approximately 6 kg of the notified chemical will be generated during the reformulation process and from empty end-user containers. These wastes will go to landfill while the rest will ultimately be released to the environment via reformulation equipment wash water or domestic wash water.

If all of the reformulation equipment wash water were discharged from either the Preston or Hornsby sites it will end up in a small STP (sewage treatment plant), which handles approximately 6 ML/day. The resultant receiving waters PEC (predicted environmental concentration) would be:

Quantity of waste notified chemical (NC)	4.5 kg/year
Number of days per year NC used	4
Capacity of STP	6 ML/day
Dilution	1:10
PEC	4.5/(4x6x10) = 0.019 mg/L

In a worst case scenario, if a full reformulation batch was disposed of to sewer at either the Prestons or Hornsby sites the resultant receiving water PEC would be:

Quantity of waste NC	2.5% of 650 kg = 16.25 kg
Capacity of STP	6 ML/day
Dilution	1:10
PEC	16.25/(6x10) = 0.27 mg/L

The effect of the flocculant treatment and pH adjustment carried out at these sites is unclear.
If the Kingsgrove site discharged all of the reformulation equipment wash water it is likely to enter the Malabar STP and the resultant PEC in the receiving waters would be in the order of 0.3 ppb.

No indication of retention by the skin has been provided, so it is presumed that all of the applied product (95.5% of the total) will ultimately enter the sewer through washing. The resultant PEC in receiving waters assumes there is no removal during treatment or adsorption in soil/sediment:

Quantity of notified chemical released	95.5% of 300 kg = 286.5 kg
Population of Australia	18 000 000
Volume of water used per person per day	150 L
Number of days	365
Dilution	1:10
PEC	286.5/(150x18 000 000x365x10) = 0.00003 mg/L (0.03 ppb)

While these PEC calculations, except for the unlikely worst-case scenario, are relatively low, the toxicity and persistence/fate of the substance are unclear. However, due to the low quantities to be imported, and the diffuse release to the aquatic component, it is unlikely that this chemical will pose a hazard to the environment, if it is used as specified by the notifier in the submission.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical is the sodium salt of a phosphodiester or ascorbic acid and cholesterol, which are common to plants and animals, are typically found in the human diet, and play key roles in several biological functions.

The notifier provided toxicological studies in support of the application for an assessment certificate. However, most of the data provided were of poor quality and employed a number of inadequately validated *in vitro* assays. Acute oral toxicity values for the components were obtained from the literature. The components have very low acute oral toxicity in rats (LD_{50} 11.9 g/kg) and in mice (LD_{50} 3 400 mg/kg). Acute dermal and inhalation studies have not been conducted on the notified chemical. Skin irritation studies conducted in humans suggest that the notified chemical is a minimal skin irritant. Eye irritation studies suggest that the notified chemical is a moderate eye irritant at 100% and mild to moderate irritant at typical use (2.5%) in cosmetic lotion vehicles; although, the data were insufficient to determine a health effects classification. There was no evidence of skin sensitisation potential and photosensitisation reactions of the notified chemical in human volunteers. No repeat dose studies were submitted for evaluation. The notified chemical was considered non-mutagenic to the bacterial strains tested and non-clastogenic *in vitro* in mammalian cells. Based on the limited toxicological data submitted, the notified chemical cannot be classified as a hazardous substance according to the NOHSC *Approved Criteria for Classifying Hazardous Substance* (National Occupational Health and Safety Commission, 1999).

Occupational Health & Safety

The notified chemical is imported as a powder with average particle size range of 10 to 15μm (but containing both inspirable and respirable particles). The notifier did not indicate whether or not an anti-dusting agent is incorporated. The inhalation toxicity and vapour pressure of the notified chemical are unknown. There is potential for chemical dispensers to be exposed by skin contact and inhalation of chemical dust during weighing and feeding the mixing tank prior to manufacture of cosmetic products. During these activities, the use of personal

protective equipment such as gloves, safety glasses, hair covering and facemasks is required. Implementation of good manufacturing safety practices for dusts, i.e., appropriate control and monitoring of ventilation and, where necessary, proper use of dust masks or other personal ventilation equipment, will be needed to ensure worker health and safety. Because inhalation exposure is of concern, employers must ensure that the NOHSC exposure standard for inspirable dust of 10 mg/m^3 time weighted average (TWA) is not exceeded in the workplace (National Occupational Health and Safety Commission, 1995). Also, care should be observed to minimise generation of chemical dust since the notified chemical contains respirable particles.

The formulation of the finished cosmetic product is carried out in a closed mixing tank. The low toxicity and concentration (2.5%) of the notified chemical in the finished product renders a low risk of adverse health effects for workers involved in the formulation and filling process, even should exposure to the chemical occur. In addition, these workers will be wearing personal protective equipment. Laboratory workers involved in formulation trials and quality testing may also come in contact with the chemical powder and the diluted product containing the notified chemical, respectively. Laboratory equipment such as fume hoods, and protective clothing should be used.

Public Health

Products containing the notified chemical will be sold to the public to be used as skin cosmetics. Dermal exposure to products containing the notified chemical is likely to occur on a daily basis, with possible accidental ocular exposure also likely. Although, the extent to which the notified chemical may be absorbed via skin is not known, systemic exposure is likely to be low due to the low concentration of the notified chemical in the end-use products. Although the quantity of the data submitted was poor, it appears that cosmetic products containing the notified chemical are not likely to present a significant hazard with respect to skin irritation, skin sensitization or photosensitisation in humans. Since insufficient *in vivo* data was supplied, the potential for the notified chemical to induce eye irritation cannot be determined. However, on the basis of the information supplied, it appears that, at concentrations likely to present in cosmetic products, the notified chemical is likely to be a slight eye irritant. Given the low concentration of the notified chemical in end-use products and the low acute toxicological hazard, the notified chemical is likely to present a low risk to public health.

13. RECOMMENDATIONS

To minimise occupational exposure to AVC-10 the following guidelines and precautions should be observed:

- A closed system or local exhaust ventilation should be applied when handling the notified chemical in powder form;
- Avoid generation of dust clouds. Employers should ensure that the NOHSC exposure standard for inspirable dust of 10 mg/m^3 TWA is not exceeded in the workplace.
- Where engineering controls not sufficient to control exposure, the following personal protective equipment is required: gloves, safety glasses, hair covering and dust mask;

- Spillage of the notified chemical should be avoided. Spillages should be swept up promptly and placed into containers for disposal;

- A copy of the MSDS should be easily accessible to employees.

Guidance in selection of protective eyewear may be obtained from Australian Standard (AS) 1336 (Standards Australia, 1994) and Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992); for industrial clothing, guidance may be found in AS 3765.2 (Standards Australia, 1990); for impermeable gloves or mittens, in AS 2161.2 (Standards Australia/ Standards New Zealand, 1998); for respirators, in AS/NZS 1715 (Standards Australia/ Standards New Zealand, 1994b) and AS/NZS 1716 (Standards Australia/ Standards New Zealand, 1994c); or other internationally acceptable standards.

14. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical was provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (National Occupational Health and Safety Commission, 1994).

This MSDS was provided by the applicant as part of the notification statement. It is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of the applicant.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Secondary notification under subsection 64(1) of the Act may be required if:

i) the method of use changes in such a way as to greatly increase the environmental exposure of the notified chemical, particularly to natural waters; or
ii) additional information becomes available on adverse environmental effects of the chemical; or
iii) the quantity of imported chemical is increased to greater than one tonne; the notifier will be required to submit a notification with complete data on physico-chemical properties, ecotoxicity and fate (including biodegradation) in accordance with the Schedule (Part B and Part C) of the Act.

Secondary notification be required if any of the circumstances stipulated under section 64(2) of the Act arise. No other specific conditions are prescribed.

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