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# NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

# **FULL PUBLIC REPORT**

**Polymer in UCAR POLYPHOBE 200 SERIES** 

This Assessment has been compiled in accordance with the provisions of the Industrial Chemicals (Notification and Assessment) Act 1989 and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by Worksafe Australia which also conducts the occupational health & safety assessment. The assessment of environmental hazard is conducted by the Department of the Environment, Sport, and Territories and the assessment of public health is conducted by the Department of Human Services and Health.

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Director Chemicals Notification and Assessment

# **FULL PUBLIC REPORT**

# **Polymer in UCAR POLYPHOBE 200 SERIES**

# 1. <u>APPLICANT</u>

Union Carbide Chemicals (Australia) Pty Ltd, Suite 1, 1st Floor, 1-7 Jordon Street, Gladesville NSW 2111

# 2. IDENTITY OF THE CHEMICAL

Based on the nature of the chemical and the data provided, the new polymer in UCAR POLYPHOBE 200 SERIES is considered to be non-hazardous. Therefore, the chemical name, CAS number, molecular formula, structural formula, molecular weight, spectral data and monomer composition have been exempted from publication in the Full Public Report and the Summary Report.

**Trade name:** UCAR POLYPHOBE 200 SERIES

Number-average molecular weight: >1000

Maximum percentage of low molecular weight species (molecular weight < 1000): 2

# 3. PHYSICAL AND CHEMICAL PROPERTIES

The notified polymer is imported as a 25% colloidal dispersion of polymer particles in water and additives. The following data refer to the polymer emulsion except where indicated.

Appearance at 20°C and 101.3 kPa: homogeneous, white milky liquid (the dried polymer is

a white solid

**Odour:** no inherent odour

**Melting Point:** no melting point was observed when the dried polymer

was heated up to 300°C

**Boiling Point:**  $100^{\circ}$ C (water)

**Specific Gravity:** 1.04 g/cm<sup>3</sup> (emulsion)

1.22 g/cm<sup>3</sup> (residue after drying)

**Vapour Pressure:** equal to water for the emulsion; expected to be

negligible for the dried polymer

Water Solubility: the presence of free acid groups should lead to

relatively high water solubility; a related polymer had a

water solubility of 0.6 g/L

**Partition Co-efficient** determined by HPLC to be 5.64 for the main

(n-octanol/water) log Po/w component of the dried polymer, however the method

was considered questionable for this surface active

polymer

**Hydrolysis as a function of pH:** not measured; the related polymer showed no change

between pH 1 and 6.5 and swelled colloidal particles

between pH 6.5 and 9

**Adsorption/Desorption:** not measured; polymers of this type are expected to

bind strongly to soil, particularly after drying

**Dissociation Constant** 7.58 (emulsion); could not be measured for

**pKa**: the dried polymer due to low water solubility

Flash Point: no flash point when tested up to 110°C (emulsion)

Flammability Limits: emulsion and dried polymer are not flammable

**Autoignition Temperature:** no self-ignition observed between 30°C and 420°C

(dried polymer)

**Explosive Properties:** emulsion and dried polymer do not detonate when

subjected to heat, shock or friction

**Reactivity/Stability:** no known reactivity, no hazardous polymerisation

expected

Particle size distribution: not required as the polymer will always be in solution

#### **Comments on physico-chemical properties:**

The polymer is unlikely to undergo hydrolysis under environmental conditions, despite the presence of carboxylic ester and carbamate functionalities.

# 4. PURITY OF THE CHEMICAL

The notified polymer contains no impurities at levels necessary to classify it as a hazardous chemical (1). Therefore, information on the purity of the polymer has been exempted from publication in the Full Public Report and the Summary Report.

# 5. INDUSTRIAL USE

The notified polymer will be imported as a component of aqueous emulsions, UCAR POLYPHOBE 200 SERIES, which will be used as thickeners and flow control agents for water-based formulations. Potential users of the polymer emulsions are expected to be manufacturers of paper (50%), paint (20%), latexes (15%), adhesives (10%) and other products (5%). Paper products will include clay-coated paper and clay-coated paperboard to be used as base stocks for printed sheet and roll stock. Paint products will be used for both domestic and commercial applications. The notified chemical will be imported at a rate of >1 tonne/annum.

# 6. OCCUPATIONAL EXPOSURE

The future customers of the notified chemical have not been confirmed, therefore the notifier was unable to provide specific details on worker exposure for each application.

In general, the notified polymer is expected to be handled in the following way. The notified polymer will be imported into Australia in metal drums as a 25% colloidal dispersion of polymer particles in water. It will be transported to Union Carbide and later distributed to potential customers for reformulation. Exposure during transportation is expected to result only in the event of accidental spills or mishandling.

At each customer site the polymer solution will be transferred from the drums and added to reformulation equipment. Once the notified polymer is reformulated it will contain a maximum of 5% polymer solution (1.25% notified polymer).

The type of equipment used will depend on the industry. It is expected that reformulation will be conducted in closed physical mixing systems, such as covered vessels with agitators. An estimated total of 20 customer manufacturing lines is proposed, involving a maximum of 2 workers exposed for 2 hours/day/shift/manufacturing line. Up to 3 shifts are envisaged per/day/site. Domestic paint products will be applied by brush, roller or spray, whereas machine coating or dipping (in addition to spray) will be utilised for commercial application. Exposure of painters and decorators will occur during product application as well as during equipment wash—up. In most cases industrial paint application will be mechanised and conducted in a ventilated and/or enclosed system.

# 7. <u>PUBLIC EXPOSURE</u>

Public exposure to the notified polymer is not expected to occur during its distribution or reformulation.

Industrial use of paints containing the notified polymer is unlikely to result in public exposure, as paint application will be under controlled conditions, and minimal waste is anticipated. Any overspray from spray booths is expected to be scrubbed prior to release to the atmosphere. Non-industrial use of paints containing the notified polymer may be extensive and the application methods used (spray, brush or roller) suggests that inhalational or dermal exposure may occur.

The methods of application for other reformulated products include 'machine' (paper and adhesives) and batch blending (latexes). Details of the different methods have not been provided and the potential for public exposure to the notified polymer, therefore, is not known.

Public exposure resulting from disposal of any waste polymer by landfill or incineration is not expected to occur.

Information on the type of 'end—use' products containing the notified polymer that the public will be able to purchase is limited, however, paper and paperboard products will be used for food

packaging. Public exposure to the notified polymer resulting from use or contact with 'end—use' products is expected to be minimal as when the water—based reformulated product cures, the polymer becomes 'bound into and becomes an integral part of the matrix'.

# 8. <u>ENVIRONMENTAL EXPOSURE</u>

#### Release

Formulation, handling and disposal

The polymer in Polyphobe 200 Series will be formulated at potentially twenty different manufacturing plants, and the process is a simple blending followed by filtration and packaging. An estimate of waste generated due to spills and formulation wastes was not given; however, it could be expected that a relatively low amount of waste would be generated annually at each formulation plant.

The primary need for disposal will occur with unused inventory or product which is spoiled by freezing or microbial attack, in which case the emulsion may be incinerated, or landfilled after the addition of absorbents for consolidation.

Details of the disposal of articles coated with paint, adhesives etc. containing the polymer were not provided.

#### Use

The polymer will initially be used in a variety of products which will result in immobilisation of the bulk (at least 94%) through incorporation in an inert coating. Up to 5% may find its way to landfill with container residues and an estimated 1-2% will be highly diluted and washed into drains around Australia when brushes, spray equipment and rollers when domestic paints containing the polymer are cleaned. The commercial paints are applied by machine coating or dip techniques which have minimum wastage.

#### **Fate**

Most of the polymer will be used as surface coating on a variety of products. The polymer used as a paper coating is likely to be disposed of at landfill or by recycling of the paper products. The cured polymer should not be mobilised during the recycling process and be contained within the sludge. When used in paints, a low percentage of the polymer could be discharged to sewer, where it may remain in colloidal suspension or be removed with sludge during treatment. Due to the low solubility and high ~ow of the polymer, the majority is expected to be adsorbed to the sludge and be disposed of by landfill or incineration. Any of the notified substance that is not absorbed will be discharged to the wider aquatic environment where it will be adsorbed to sediment and suspended particulates and likely to persist despite the presence of carboxylic ester and carbamate linkages. However, possibilities such as oxidative cleavage of the polyether chain or ester hydrolysis indicate that the polymer may eventually degrade.

Similar considerations lead to the expectation that residues consigned to landfill will slowly degrade. Significant leaching appears unlikely, although the notified substance, as a colloidal suspension, may move with bulk water flow.

# 9. EVALUATION OF TOXICOLOGICAL DATA

Although not a requirement under the *Industrial Chemicals (Notification and Assessment) Act 1989*, toxicological data were provided for the notified polymer. The test substance used in the following studies was UCAR POLYPHOBE THICKENER 205, either as a white milky emulsion containing 25% notified polymer in water, or as clear yellowish fragments of dry polymer.

# 9.1Acute Toxicity

Table 1 Summary of the acute toxicity of notified polymer

Test	Species	Outcome	Reference
Oral	Rat	LD <sub>50</sub> >2000 mg/kg	2
Dermal	Rat	LD <sub>50</sub> >2000 mg/kg	3
Skin Irritation	Rabbit	non irritant	4
Eye Irritation	Rabbit	slight irritant	5
Skin Sensitisation	Guinea pig	non sensitising	6

# 9.1.1

### Oral Toxicity (2)

This study was conducted in accordance with OECD guideline No: 401 (7)

The polymer emulsion was administered by oral gavage to 20 Wistar rats (5/sex/dose) at effective polymer doses of 500 or 2000 mg/kg (1.9 and 7.62 ml/kg body weight respectively). Clinical observations were made over a 15-day period. No deaths occurred during the observation period. All rats were sacrificed on day 15 and necropsy performed. The fur of 1 male treated with the low dose showed a rough coat on day one. No other clinical signs were noted. The bodyweight gains of the treated animals were unaffected by treatment in all rats except the females treated with the high dose, which showed slight decrease in bodyweight gain over the second week. Necropsy on sacrificed animals revealed no significant macroscopic lesions.

Results of this study indicate an acute oral  $LD_{50}$  of >2000 kg/mg in rats for the notified polymer.

#### 9.1.2

# **Dermal Toxicity (3)**

This study was conducted in accordance with OECD guideline No: 402 (8)

The polymer emulsion was applied at effective polymer doses of 500 or 2000 mg/kg (1.9 and 7.62 ml/kg body weight respectively) to the clipped backs of 20 Wistar rats (5/sex/dose) and covered with an occlusive dressing. Twenty-f our hours later the dressing was removed and the test site washed with tissue soaked with tap-water. Clinical observations were made at 24 hours and over a 15 day

period. No deaths occurred during the observation period. All rats were sacrificed on day 15 and necropsy performed.

Lethargy was noted on day 1 in two males treated with the low dose. Erythema was noted on the skin of four females (one with scabs) after treatment with the high dose. Erythema and scabs were noted in one male after low dose treatment. Effects on body weight gain were noted in all animals treated with the high dose and three females treated with the low dose. Necropsy on sacrificed animals revealed no significant macroscopic legions.

Results of this study indicate an acute dermal  $LD_{50}$  of >2000 kg/mg in rats of both sexes for the notified polymer.

# 9.1.3 Skin Irritation (4)

This study was conducted in accordance with OECD guideline No: 404 (9)

A single dose of 0.5 g dry polymer (ground to a fine powder and moistened with bi-distilled water) was applied by semi-occlusive application to one shaved flank of 3 male New Zealand white rabbits. The opposite flank of each animal was treated in the same manner except for the omission of the test substance. Four hours later the dressings were removed and the test site wiped with moistened tissue. Skin reactions were assessed 1, 24, 48 and 72 hours after dressing removal. No clinical symptoms or mortality were observed in the animals during the 72 hour observation period. One animal showed a red spot (covering 5% of the treated area) on day 2. This was not considered to be related to treatment. No other skin reactions were observed over the observation period.

Results of this study indicate that the notified polymer is not a skin irritant in rabbits.

# 9.1.4 Eye Irritation (5)

This study was conducted in accordance with OECD guideline No: 405 (10).

A single dose of 0.1 g of dry polymer (ground to a fine powder and moistened with bi-distilled water) was instilled in the conjuctival sac of one eye of each of 3 New Zealand white rabbits. The other eye served as the control. The eyes were examined 1, 24, 48 and 72 hours after treatment. All treated eyes showed slight conjunctival redness at the 1 and 24 hour observations. This effect persisted in one animal to 48 hours. No corneal opacity was observed in any of the animals during the study. Conjuctival chemosis was observed in 1 animal at 24 hours only. Treatment of the eye with 2% fluorescein revealed no epithelial damage 24 hours after instillation of the test substance. No corrosion was observed. No deaths occurred and no clinical symptoms were observed during the study.

The results of this study suggest that notified polymer is a slight eye irritant in rabbits.

#### 9.1.5 Skin Sensitisation (6)

This study was conducted in accordance with OECD guideline No: 406 (11).

The Magnusson-ligman Maximisation Test was used. Test animals were albino guinea pigs.

### **Preliminary study**

One guinea pig was injected intradermally (in 4 sites of clipped shoulder region) with 0.1 ml of 5% (w/w) concentration of the polymer emulsion in distilled water. The skin reactions were assessed 24 and 48 hours later.

The same animal was treated topically (on shaved left flank) with 0.5 ml undiluted polymer

emulsion. Similar applications were made in 4 other animals with 0.05 ml undiluted, 50%, 25% and 10% (w/w) emulsion. The test sites were occluded for 24 hours. Skin reactions were assessed 24 and 48 hours after patch removal.

Based on the preliminary study, an intradermal induction dose of 2.5% (w/w) and an epidermal induction dose of 100% (w/w) were chosen for the main study. Challenge doses chosen were 100%, 50%, and 25% (w/w).

# Main study

#### Induction

On day 1, 20 test animals (sex not specified) were injected intradermally (on either side of a 4 x 6 cm clipped area of the dorsal scapula) with 0.1 ml Freund's Complete Adjuvant diluted 50:50 with physiological saline (50:50 FCA), 2.5% (w/w) emulsion in physiological saline and 2.5% (w/w) emulsion in 50:50 FCA. Similar injections were made in the 10 control animals without the test material.

On day 6, all animals were induced by massaging 10% sodium dodecyl sulphate in petroleum oil into the clipped and shaved dorsal scapular region. The following day, a patch was applied with 0.5 ml undiluted emulsion to the test animals (between the injection sites) and covered with a dressing for 48 hours. Control animals were treated as above with the omission of the test substance. Skin reactions were assessed by the Draize method immediately after patch removal.

Slight to severe erythema or signs of necrosis and slight to moderate oedema were observed in 17/20 test animals. Of the control animals 9/10 showed slight erythema and 6 of these also showed well-defined oedema.

# Challenge

Two weeks after the epidermal induction application, the shaved left flank of each guinea pig received 4 patches: 100%

emulsion, 50% emulsion, 25% emulsion and vehicle (distilled water) alone. The patches were occluded for 24 hours after which the test sites were wiped with moistened tissue to remove residual test substance. Sensitisation reactions were assessed 24 and 48 hours after patch removal.

No skin reactions were observed in 19/20 test animals and 10/10 control animals at either 24 or 48 hours after any of the challenge doses. In the remaining test animal red spots observed only at 24 hours after treatment with undiluted emulsion.

The results of this study suggest that the notified polymer is not a skin sensitiser in guinea pigs.

# 9.3 Genotoxicity

#### 9.3.1 Salmonella typhimurium Reverse Mutation Assay (12)

This study was conducted in accordance with OECD guideline No: 471 (13).

The notified polymer (dissolved in dimethylsulfoxide) was tested in a *Salmonella typhimurium* reverse mutation assay using the direct plate incorporation procedure in the test strains TA 98, TA 100, TA 1535 and TA 1537, with or without metabolic activation.

Two experiments were conducted, each in triplicate. All strains were tested with the test substance at concentrations of 0, 100, 333, 1000, 3330 or 5000 ag/plate. The reference mutagens daunomycin (TA 98; - S9), methylmethanesulfonate (TA 100; - S9), sodium azide (TA 1535; - S9), 9-aminoacridine (TA 1537; - 59) and 2-aminoanthracene (all strains; + S9) were used as positive controls and gave the expected responses.

In both experiments there were no increases in the revertant colony number above control level in any of the strains in the presence or absence of metabolic activation.

Under the experimental conditions reported, the notified polymer was found not to be mutagenic.

# 9.3.2 Chromosome Aberrations in Cultured Peripheral Human Lymphocytes (14)

This study was conducted in accordance with OECD guideline No: 473 (15)

Experiments were conducted in duplicate. Human lymphocytes were exposed to the notified polymer (dissolved in dimethylsulfoxide) with and without exogenous metabolic activation. Concentrations of 0, 10, 33, 100 and 333 ~.tg/ml culture medium were incubated with S9 mix and harvested at 24 hours (all concentrations) or 48 hours (333 Jhg/ml only). Cultures without S9 mix were treated with 0, 33, 100, 178 and 333 ~tg/ml and harvested at 24 hours (all concentrations) and 48 hours (333 ~g/ml only). Cells were also treated with the reference mutagens cyclophosphamide (+ S9) and mitomycin C (- S9) and harvested at both 24 and 48 hours. All cultures containing S9 were rinsed after 3 hours incubation and fresh growth media added. Colchicine was added during the last 3 hours of incubation to arrest the cells at metaphase. Two slides were prepared for each culture.

Stained chromosome preparations were examined for chromosomal aberrations (at least 100 metaphases per treatment group).

Both in the presence and absence of metabolic activation, the notified polymer did not induce any significant increases in the number of cells with chromosome aberrations.

Under the conditions of this test the notified polymer in not clastogenic *in vitro*.

# 9.2 Overall Assessment of Toxicological Data

Animal tests suggest that the notified polymer has low acute oral and dermal toxicity (rat  $LD_{50}s > 2000 \text{ mg/kg}$ ) and is not a skin irritant or sensitiser. It is a slight eye irritant. However, the slight eye irritation may have resulted from the abrasive nature of the polymer in powder form.

Genotoxicity studies indicate that the chemical does not cause point mutations in *Salmonella typhimurium* and is not clastogenic in human peripheral lymphocytes.

# 10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Ecotoxicity testing is not normally required for high molecular weight polymers as they are not transported readily across biological membranes and thus cannot affect living organisms. However, the company has provided available ecotoxicity data in its proposal, as required by the *Industrial Chemicals (Notification and Assessment) Act 1989*.

Information of the toxicity of the polymer emulsion was provided for fish (carp) and *Daphnia Magnia*. The tests were performed in accordance to the OECD guidelines No. 202 (Daphnia) and No. 203 (fish). At a concentration of 1000 mg/L (nominal) no toxic effects to either carp or daphnia were observed. The actual concentrations were within 10% of the nominal at the start and finish of the tests. However, one test (out of three) with the carp showed a significant change between the start (998/1002 mg/L) and the final (733/735 mg/L). It is likely that at these concentration of the polymer was only partially soluble, with the remainder dispersed.

Polymers with free carboxylic acid functions are known to be moderately toxic to green algae (16), especially those with large numbers of free carboxylic acids. The toxicity values range from 1-100 ppm, depending on the number of carboxylic acids that are free. Polyphobe 200 series could therefore be slightly to moderately toxic to green algae.

# 11. <u>ASSESSMENT OF ENVIRONMENTAL HAZARD</u>

The notified substance is a high molecular weight polymer with minimal chemical reactivity and no obvious ecotoxicological potential. It will be used in aqueous based coating products and become essentially immobile after incorporation in the dried coatings. Small amounts could be discharged to sewers around Australia when paint brushes, rollers and spray equipment is washed, which will then be treated at municipal treatment works. Assuming that 2% of the polymer which is used in paints is discharged to sewers around Australia, 4 tonnes per annum of polymer could be discharged. For a metropolitan area of 1 million people and 300 ML of sewage discharge per day (average figures for Australia) with average release of polymer from paints per capita and all of the polymer is discharged to the environment, 2 ppb of polymer could be discharged per day. This is well below the toxic levels to fish and daphnia and that expected for green algae. Further, the majority of the polymer will be contained in the sludge and disposed of by incineration or at landfill. Any polymer that leaves the sewage plant will be highly diluted, resulting in widespread but low level environmental exposure of the aquatic compartment. The predicted environmental hazard is minimal.

# 12. <u>ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS</u>

The notified polymer has a NAMW > 1000 and is therefore unlikely to cross biological membranes and cause significant systemic effects. The polymer contains -2% (w/w) low molecular weight (<1000) species and a total of -0.5% hazardous residual monomers/reactants. The concentration of each impurity however, is below the cut—off concentration for classifying the polymer as a hazardous substance (1).

The polymer, which will be available in Australia as an emulsion only, is stable at room temperature, not flammable and not known to react with other chemicals.

Animal tests indicate eye irritation to be the major health effect associated with polymer exposure. However, the observed eye irritation may have been due to the abrasive nature of the polymer powder.

Under normal use conditions, workers involved in reformulating the polymer will be required to use appropriate engineering controls and personal protective equipment to minimise exposure to hazardous components in the formulations. As a consequence, exposure to the notified polymer should be minimal during these operations.

The potential for exposure (particularly eye and skin contact) will be greater among workers applying products containing the polymer, such as painters and decorators applying domestic and commercial paints. Given the low concentration of the notified polymer in these products and the low hazard associated with the polymer, the notified chemical is not expected to present a significant health or safety risk to these workers.

While public contact with the notified polymer may be significant, exposure levels will be low and as the notified polymer has a high NAMW absorption is unlikely to occur.

Under normal use conditions, any risks associated with the use of polymer should be minimal.

### 13. RECOMMENDATIONS

To minimise occupational exposure to the notified polymer the following guidelines and precautions should be observed.

- If engineering controls and work practices are insufficient to reduce exposure of the notified polymer to a safe level, the following personal protective equipment should be used:
- safety spectacles with side shields or other suitable eye protection conforming to Australian Standards 1336 (17) and 1337 (18);
- impervious gloves conforming to Australian Standard 2161 (19); and
- protective clothing conforming to Australian Standards 3765.1 (20) or 3765.2 (21).
- Good work practices should be implemented to avoid splashings or spillages during formulation and use of products.
- Spills should be cleaned up promptly.
- Good personal hygiene practices, such as washing of hands prior to eating food, should be observed.
- A copy of the MSDS for products containing the notified chemical should be easily accessible to all employees.

# 14. MATERIAL SAFETY DATA SHEET

The Material Safety Data Sheet (MSDS) for UCAR POLYPHOBE 205/UCAR POLYPHOBE 206 (Attachment 1) was provided in Worksafe Australia format (22). The MSDS was provided by Union Carbide Chemicals (Australia) Pty Ltd as part of their notification statement. It is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of Union Carbide Chemicals (Australia) Pty Ltd.

# 15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the *Industrial Chemicals (Notification and Assessment) Act 1989*, secondary notification of the polymer in UCAR POLYPHOBE 200 SERIES shall be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

# 16. <u>REFERENCES</u>

- 1. National Occupational Health and Safety Commission, *Guidance Note for Determining and Classifying a Hazardous Substance*, Australian Government Publishing Service Publ., Canberra, 1991.
- 2. RCC NOTOX Project 075893. Assessment of Acute Oral Toxicity with UCAR Polyphobe Thickener 205, 25% in the Rat. Research and Consulting Company By, The Netherlands, 1993.
- 3. RCC NOTOX Project 075904. Assessment of Acute Dermal Toxicity with UCAR Polyphobe Thickener 205, 25% in the Rat. Research and Consulting Company By, The Netherlands, 1993.

- 4. RCC NOTOX Project 075915. Primary Skin Irritation/Corrosion Study with UCAR Polyphobe Thickener 205, 25% in the Rabbit (4-Hour Semi-Occlusive Application). Research and Consulting Company By, The Netherlands, 1993.
- 5. RCC NOTOX Project 075926. Acute Eye Irritation/Corrosion Study with UCAR Polyphobe Thickener 205 in the Rabbit. Research and Consulting Company By, The Netherlands, 1993.
- 6. RCC NOTOX Project 075937. Assessment of Contact Hypersensitivity to UCAR Polyphobe Thickener 205, 25% in the Albino Guinea Pig (Maximization-Test). Research and Consulting Company By, The Netherlands, 1993.
- 7. OECD Guidelines for Testing of chemicals *Acute Oral Toxicity* No: 401, 1981.
- 8. OECD Guidelines for Testing of chemicals *Acute Dermal Toxicity* No: 402, 1981.
- 9. OECD Guidelines for Testing of Chemicals *Acute Dermal Irritation/Corrosion* No: 404, 1981.
- 10. OECD Guidelines for Testing of chemicals Acute Eye Irritation/Corrosion No: 405, 1987.
- 11. OECD Guidelines for Testing of chemicals Skin Sensitisation No:406, 1981.