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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

Silane Modified Colloidal Silica in Water Dispersion (Levasil CC Series)

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of the Environment and Energy.

This Public Report is available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

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Director
NICNAS

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SUMMARY

The following details will be published in the NICNAS *Chemical Gazette:*

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1576	AkzoNobel Chemicals Australia Pty Ltd Chemcolour Industries Australia Pty Limited Ezi Floor Products (Vic) Pty Ltd Bonakemi Australia Pty Ltd	Silane Modified Colloidal Silica in Water Dispersion (Levasil CC Series)	ND*	≤ 150 tonnes per annum	Component of industrial coatings, industrial cleaning products and construction products

*ND = not determined

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
As only limited toxicity data were provided, the notified chemical cannot be classified according to the *Globally Harmonised System of Classification and Labelling of Chemicals* (GHS), as adopted for industrial chemicals in Australia.

Human health risk assessment
Provided that the recommended controls are being adhered to, under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

When used in the proposed manner, the notified chemical is not considered to pose an unreasonable risk to public health.

Environmental risk assessment
On the basis of the currently available information about the aquatic hazards of silica nanomaterials and assessed use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment. However, if additional hazard information becomes available to indicate that the notified chemical has hazard characteristics of concern for the environment, then the risks posed by industrial uses of the notified chemical will need to be re-assessed.

Recommendations

REGULATORY CONTROLS

Health Surveillance

- As the manufactured notified chemical may present as nano-size particles (< 100 nm) in water dispersions, there are uncertainties for its potential to cause adverse health effects. Employers should carry out health surveillance for workers who have been identified in the workplace assessment as having significant risk of exposure to the manufactured notified chemical.

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls at reformulation sites to minimise occupational exposure to the notified chemical as introduced in water dispersions:
  - Enclosed/automated systems where possible
  - Local exhaust ventilation

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling products containing the notified chemical:
  - Avoid generation of aerosols at all time
  - Avoid contact with skin and eyes
  - Avoid inhaling aerosols if generated

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced in water dispersions for use in industrial products:
  - Protective clothing
  - Impervious gloves
  - Safety glasses or goggles
  - Respiratory protection if aerosol generation is expected

  Selected personal protective equipment should be capable of protecting workers from exposure to nano-size particles. Guidance in selection of personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)* as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Disposal

- Where reuse or recycling are not appropriate, dispose of the notified chemical in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

Storage

- The handling and storage of the notified chemical should be in accordance with the Safe Work Australia Code of Practice for *Managing Risks of Hazardous Chemicals in the Workplace* (SWA, 2012) or relevant State or Territory Code of Practice.

Emergency procedures

- Spills and/or accidental release of the notified chemical should be handled by physical containment, collection and subsequent safe disposal.

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the

notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if
- the importation volume of the notified chemical exceeds 150 tonnes per annum;
- the end use concentration of the notified chemical in industrial cleaning products exceeds 5%;
- the notified chemical is intended to be used in products available to the public;
- the notified chemical is intended to be used in products involving spray application;
- additional information has become available to the person as to an adverse effect of the notified chemical due to nano-size particle properties on human health or the environment;
- additional information has become available to the person as to the environmental fate of the notified chemical due to nano-size particle properties, in relation to partitioning behaviour, including the fate during wastewater treatment processes;

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a component of industrial coatings, industrial cleaning products and construction products, or is likely to change significantly;
- the amount of chemical being introduced has increased, or is likely to increase, significantly;
- the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

AICS Annotation

- When the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS) the entry is proposed to be annotated with the following statement:
  - This chemical has been assessed by NICNAS and there are specific secondary notification obligations that must be met. Potential introducers should contact NICNAS before introduction.

Safety Data Sheet
The SDS of products containing the notified chemical provided by the notifier were reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANTS
AkzoNobel Chemicals Australia Pty Ltd (ABN: 64 621 806 273)
8 Kellaway Place
WETHERILL PARK NSW 2164

Chemcolour Industries Australia Pty Limited (ABN: 70 125 602 271)
20-22 Gardiner Road
NOTTING HILL VIC 3168

Ezi Floor Products (Vic) Pty Ltd (ABN: 22 087 581 520)
9/1866 Princes Highway
CLAYTON VIC 3168

Bonakemi Australia Pty Ltd (ABN: 35 096 221 448)
c/o Nexia Court & Co
21 Beaconsfield Parade
LINDFIELD NSW 2070

NOTIFICATION CATEGORY
Standard: Chemical other than polymer (more than 1 tonne per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: chemical name, CAS number, molecular and structural formulae, molecular weight, analytical data, degree of purity, impurities, additives/adjuvants, analogue information, use details and import volume.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows: boiling point, vapour pressure, water solubility, hydrolysis as a function of pH, adsorption/desorption, dissociation constant, auto ignition temperature, explosive properties, oxidising properties, acute oral toxicity, acute dermal toxicity, skin irritation, eye irritation, repeated dose toxicity, genotoxic damage *in vivo*, ready biodegradation, bioaccumulation, fish acute toxicity, *Daphnia* acute immobilisation/reproduction and alga growth inhibition.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
Canada (2015)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Levasil CC Series (water dispersions containing the notified chemical at < 50%), including:

- Levasil CC 151 (previously Bindzil CC 151)
- Levasil CC 301 (previously Bindzil CC 301)
- Levasil CC 302 (previously Bindzil CC 302)
- Levasil CC 401 (previously Bindzil CC 401)

(Marketing names of products containing the notified chemical changed from Bindzil CC series to Levasil CC series during the assessment. In this report, the notified chemical is assessed as in Bindzil CC series. The notifier has indicated that except for the name changes there is no difference between Bindzil CC series and Levasil CC series.)

OTHER NAME
Silane Modified Colloidal Silica in Water Dispersion (chemical characterisation included in Safety Data Sheet)

MOLECULAR WEIGHT
Number Average Molecular Weight (Mn) > 10,000 Da

ANALYTICAL DATA
Reference NMR spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
> 95%

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 °C AND 101.3 kPa: clear to cloudy aqueous dispersions*

Property	Value	Data Source/Justification
Melting Point/Freezing Point	Not determined	Introduced in aqueous dispersions
Boiling Point	Not determined	Introduced in aqueous dispersions
Density	Bindzil CC 151: 1,080 – 1,120 kg/m^3 Bindzil CC 301: 1,170 – 1,210 kg/m^3 Bindzil CC 302: data lacking Bindzil CC 401: 1,050 – 1,400 kg/m^3	SDS
Vapour Pressure	Not determined	Expected to be low based on molecular weight
Water Solubility	Not determined	Expected to be dispersible
Hydrolysis as a Function of pH	Not determined	Not expected to hydrolyse significantly in the environmental pH of 4 – 9
Partition Coefficient (n-octanol/water)	log Pow < -3.2^ at 20 °C	Measured
Adsorption/Desorption	Not determined	May partition to the solid phase via various mechanisms (e.g., heteroaggregation, interaction with biological material)
Dissociation Constant	Not determined	Contains ionic functional groups; expected to dissociate in the environmental pH of 4 – 9.
Flash Point#	Bindzil CC 151: > 95 °C Bindzil CC 301: 61 °C Bindzil CC 302: 53 °C Bindzil CC 401: 61 °C	Measured
Flammability	Bindzil CC 151: Not a flammable liquid Bindzil CC 301: Category 4 flammable liquid Bindzil CC 302: Category 3 flammable liquid Bindzil CC 401: Category 4 flammable liquid	Based on measured flash point
Autoignition Temperature	Not determined	Introduced in aqueous dispersions
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidative properties

* The notified chemical is produced in aqueous dispersions and never isolated.
# Bindzil CC series products contain highly flammable ethanol as additive/adjuvant.
^ This log Pow figure may not be relevant for the notified chemical in form of insoluble nano-size particles (see Appendix A).

PARTICLE SIZE DISTRIBUTION

Particle size distributions by number for the originally manufactured notified chemical in typical batches of the products are summarised in following table.

Product	*Detected Size Range (nm)*	*Z-Average Size (nm)*	*Instrument*
Bindzil CC 151	6.50 – 28.21	18.03	Malvern Zetasizer (DTS Ver. 5.03)
Bindzil CC 301	6.50 – 32.67	27.02	Malvern Zetasizer (DTS Ver. 5.03)
Bindzil CC 302	8.72 – 32.67	19.03	Malvern Zetasizer (DTS Ver. 5.03)
Bindzil CC 401	11.70 – 43.82	23.54	Malvern Zetasizer (DTS Ver. 5.03)

The manufactured notified chemical in water dispersions has typical particle size < 100 nm.

A test was conducted to determine whether the notified chemical remains in nano-size after being applied as wet films onto substrates, dried and re-dispersed in water. The samples were applied onto clean glass plates and dried for 72 hours at room temperature. The dried films were scraped off, weighted, and re-dispersed in 20 mM NaCl. The dispersions were then filtered with 5 µm pore size syringe filters. Particle size distributions of the filtered fractions were measured by dynamic light scattering (DLS) while the size distributions of the coarse fractions were measured by laser diffraction. The results showed that less than 0.3% of the mass of re-dispersed notified chemical was present in the form of particles with size < 10 µm. Particles with size < 100 nm were also detected in filtered fractions of the re-dispersed notified chemical as shown in the following table.

Product	*Mean Diameter of Fresh Material (nm)*	*Mean Diameter of Particles in Filtered Fraction (nm)*	*Mass of Particles with size < 10 µm in Coarse Fraction (%)*
Bindzil CC 151	14.66	172.4	0.09
Bindzil CC 301	16.05	229.4	0.23
Bindzil CC 302	16.38	67.58	0.16
Bindzil CC 401	18.82	34.37	0.26

After drying process, the notified chemical may produce a small portion of particles with size < 100 nm upon re-dispersion in water.

DISCUSSION OF PROPERTIES

For full details of tests on physical and chemical properties, refer to Appendix A.

The notifier also provided following information for the notified chemical in water dispersions; however, no test details were submitted:

Product	*Shape*	*pH*	*Surface Area (m^2/g)*	*SiO_2 Content (%)*	*Zeta Potential*	*Aggregate Size (µm)*
Bindzil CC 301	Spherical	8	360 ± 30	27	Negative	Not expected to aggregate
Bindzil CC 401	Spherical	8	220 ± 20	37	Negative	Not expected to aggregate

Reactivity

The notified chemical is expected to be stable under normal conditions of use. The manufactured notified chemical in nano-size may contain residual surface reactive epoxide groups; however a ^{13}C CP/MAS NMR spectroscopy conducted on freeze-dried Bindzil CC 301 indicated that the epoxide groups were not detectable by NMR. The manufactured Levasil (Bindzil) CC series products may contain highly flammable ethanol.

Physical hazard classification

Based on the submitted physical-chemical data depicted in the above table, the notified chemical is not recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

However, due to the presence of flammable additives/adjuvants in the manufactured water dispersions, the products containing the notified chemical should be classified according to GHS based on measured flash points (e.g. combustible liquid or flammable liquid and vapour). Based on the product hazard classifications, the notifiers should consider their obligations under the Australian Dangerous Goods Code (NTC 2017).

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

The notified chemical will not be manufactured in Australia. It will be imported into Australia in Levasil CC series products, including Levasil CC 151, Levasil CC 301, Levasil CC 302 and Levasil CC 401, at a maximum concentration of < 50% for reformulating into industrial coatings and construction products. The notified chemical will also be imported as a component of construction products or industrial cleaning products at a maximum concentration of < 25% or < 5%, respectively.

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	≤ 150	≤ 150	≤ 150	≤ 150	≤ 150

PORT OF ENTRY

Sydney, Melbourne, Perth and Brisbane

TRANSPORTATION AND PACKAGING

The Levasil CC series products containing the notified chemical at < 50% concentration will be packaged in 1,000 L intermediate bulk containers (IBCs) and transported within Australia by road and/or rail for distribution to reformulation sites.

Reformulated finished coating products containing the notified chemical at < 10% concentration will be packed in various size standard paint containers for distribution to industrial or commercial customer sites.

Finished industrial cleaning products containing the notified chemical at < 5% concentration will be imported in 3 L or 5 L plastic cans or in IBCs. Products in IBCs will be repackaged into 3 L or 5 L containers for further distribution. The cleaning products will be distributed by road and/or rail to industrial or commercial customers.

Reformulated and imported finished construction products containing the notified chemical at < 25% concentration will be packed in 20 – 200 L containers or IBCs and distributed to construction sites for use in concrete floor applications.

USE

The notified chemical will be used as a component of industrial coatings (at < 10% concentration), industrial cleaning products (at < 5% concentration) or construction products (at < 25% concentration). All finished products containing the notified chemical will be solely used by workers for industrial or commercial purposes. No products containing the notified chemical will be available to the public.

OPERATION DESCRIPTION

Reformulation

Industrial Coatings

At the reformulation sites, the Levasil CC series products containing the notified chemical will be manually weighed or metered directly from the imported containers into a stainless steel blending tank and mixed with other ingredients, including pigments and resin, to form the mill base. The resulting mill base will then be pumped into a large mixing vessel to which the remaining additives will be added and blended to form the finished product. Samples will be taken from the products for quality control testing by laboratory technicians. The finished coating products (contain the notified chemical at < 10% concentration) will be filled into containers by gravity from the bottom of the mixing vessel through filters and filling lines. Reformulation equipment will be cleaned by rinsing with water or solvents.

Construction Products

At the reformulation sites, the Levasil CC series products containing the notified chemical will be manually weighed directly from the imported containers into a mixing vessel. Other ingredients, including different silicates and wetting agents, will then be added and thoroughly mixed with the notified chemical. Samples will be taken from the reformulated products for quality control testing by laboratory technicians. The finished construction products (containing the notified chemical at < 25% concentration) will be filled into various

containers in sizes ranging from 20 L to 200 L by gravity from the bottom of the mixing vessel. Mixing equipment will be cleaned by rinsing with water.

Industrial Cleaning Products
No reformulation of industrial cleaning products containing the notified chemical will occur in Australia.

End Use
Industrial coating products containing the notified chemical (at < 10% concentration) will be mainly used for outdoor applications including coatings on surfaces of walls, roofs, wood and brick. The coating products will be applied by brush and roller.

Industrial cleaning products containing the notified chemical (at < 5% concentration) will be used by workers for hard surface cleaning in buildings including hospitals, schools and hotels.

Construction products containing the notified chemical (at < 25% concentration) will be used by workers in concrete floor applications including polishing, surface treatment and densification.

No spray application will be used for any product containing the notified chemical.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
General		
Stevedores	2 – 3	5
Transport and storage	4 – 8	5
Industrial Coatings		
Reformulation	4	260
Laboratory testing	4	260
Application/use	6	260
Maintenance and cleaning	8	260
Construction Products		
Reformulation	4	40
Laboratory testing	1	40
Application/use	6 – 7	260
Maintenance and cleaning	1 – 2	260
Industrial Cleaning Products		
Application/use	8	260

EXPOSURE DETAILS
Transport and storage workers are not expected to be exposed to the notified chemical except in the unlikely event of an accident.

Reformulation
For coating and construction product reformulations, dermal and ocular exposure of workers to the notified chemical at < 50% concentration may occur when weighing, metering, mixing and transferring materials containing the chemical or during laboratory testing, equipment cleaning and maintenance. Given the notified chemical will be imported in water dispersions, inhalation exposure to the chemical is not expected unless aerosols are formed during the processes. Exposure to the notified chemical is expected to be minimised through the use of enclosed and automated systems, local exhaust ventilation and suitable personal protective equipment (PPE) capable of protecting workers from exposure to nano-size particles, including impervious rubber gloves, safety glasses with side protection or goggles, protective clothing and respiratory protection (if aerosols are expected).

End Use
Workers applying coatings containing the notified chemical by rollers and brushes may have potential for dermal and ocular exposure to the chemical at < 10% concentration. Dermal and ocular exposure to the notified chemical at < 5% concentration may occur to workers using the cleaning products containing the chemical. Construction workers may come into contact with the notified chemical at < 25% concentration when using products containing the chemical to treat concrete floor surfaces.

As spray methods will not be used for any of the applications, inhalation exposure to the notified chemical is not expected to occur unless aerosols are formed during end use. The potential for dermal and ocular exposure during the applications is expected to be minimised by the use of suitable PPE including impervious gloves, safety glasses or goggles and coveralls. If there is potential for aerosol formation, respiratory protection is also expected to be used.

6.1.2. Public Exposure
Products containing the notified chemical will not be available for use by the public. Members of the public may come into contact with cured coatings and treated concrete floors containing the notified chemical or cleaned hard surfaces with residuals of the notified chemical. However, once the coatings are cured the notified chemical is expected to be bound into an inert matrix and will not be bioavailable. The construction products containing the notified chemical are also anticipated to form an inert matrix on the treated concrete floor surfaces. Residuals of the notified chemical on hard surfaces are expected to dry and are not expected to remain as nano-size particles.

After the cleaning applications using products containing the notified chemical, a proportion of the chemical is expected to be released to the environment. Available information indicates that the released notified chemical may interact with biological materials and undergo heteroaggregation in the environment to form micro-size materials. Once the aggregated notified chemical is diluted in the environment, public exposure to nano-size particles of the notified chemical after the release is not expected.

6.2. Human Health Effects Assessment
The results from toxicological investigations conducted on the notified chemical or analogue chemicals are summarised in the following table. The manufactured notified chemical in water dispersions has typical particle size < 100 nm. However, particle sizes of the test substances in the submitted study reports were not specified. For full details of the studies, refer to Appendix B.

Endpoint	*Result and Assessment Conclusion*	*Test Substance*
Rat, acute inhalation toxicity	LC50 > 5 mg/L/4 hour; low toxicity	Analogue
Mouse, skin sensitisation – Local lymph node assay	no evidence of sensitisation	Notified chemical
Mutagenicity – bacterial reverse mutation	non mutagenic	Notified chemical
Genotoxicity – *in vitro* mammalian cell gene mutation test	non genotoxic	Notified chemical

Toxicokinetics, metabolism and distribution
No specific information on toxicokinetics, metabolism and distribution was submitted for the notified chemical.

Main route of exposure during use of the notified chemical is expected to be dermal. An *in vitro* dermal absorption study report on the chemical using human epidermis models was submitted. The dermal absorption was tested on Bindzil CC 301 containing < 50% concentration of the notified chemical. Under the conditions of the test, dermal absorption of silica contents from the test substance through human epidermis was slow and negligible. Data showed that almost all applied dose was removable by washing after 24 hours of exposure (see Appendix B).

The Scientific Committee on Consumer Safety of the European Commission (SCCS) has reviewed the toxicity of various nano-forms of silica used in cosmetics and regarded current information on skin penetration of silica nanoparticles/clusters as insufficient and inconclusive (SCCS 2015). Further studies on the dermal penetration of silica nanoparticles may be required to address the uncertainties (Nafisi *et al* 2015; Ngo *et al* 2013). Based on the available information, the potential for nano-size particles of the notified chemical to be able to penetrate the skin cannot be completely ruled out.

Acute toxicity
The acute inhalation toxicity of a suitable analogue (silica with similar surface modification) was evaluated in rats. The animals were exposed nose-only to respirable aerosols of the test substance at an average concentration of 5.126 mg/L and 5.102 mg/L for 4 hours in 2 separate tests. No deaths occurred and no clinical signs were noted during the tests.

At the end of the tests, one female rat was found to have several dark foci in the lungs at the necropsy. No other organ abnormality was observed. Based on the results, the LC50 of the analogue chemical was determined to be greater than the concentrations tested (i.e., LC50 > 5.126 mg/L/4 hours and LC50 > 5.102 mg/L/4 hours in 2 separate tests), indicative of low acute inhalation toxicity under the conditions of the tests.

The notified chemical has particle size < 100 nm. Reactivity of nano-size particles is largely affected by the chemical composition of the particle surface. A correlation has been reported between the surface reactivity and pulmonary inflammation for nanoparticles (van Ravenzwaay *et al* 2009; Warheit *et al* 2007a and 2007b). The findings suggest that surface reactivity of nanoparticles may be the most important characteristics in determining the pulmonary effects (Braakhuis *et al* 2014). However, the study reports provided for the analogue chemical did not include physical-chemical characterisation of the test substance, especially the surface reactivity.

Irritation
No study reports on skin or eye irritation properties of the notified chemical were provided. SDS for products containing the notified chemical indicate that the products may cause skin and eye irritation.

Skin sensitisation
A local lymph node assay (LLNA) on mouse was conducted to assess the skin sensitization potential of Bindzil CC 301. The resulting stimulation index (SI) was < 3 when tested at the original concentration (< 50%) and the notified chemical was not considered by the study authors to be a skin sensitiser under the conditions of the assay.

Repeated dose toxicity
No repeated dose toxicity study on the notified chemical or a suitable analogue was provided.

Mutagenicity/Genotoxicity

Bacterial reverse mutation test
A bacterial reverse mutation test report for the notified chemical was submitted. The test was conducted using both *Salmonella typhimurium* and *Escherichia coli* strains. Neither concentration-related decrease in colony counts nor significant increase in the number of revertants was observed with or without metabolic activation. The notified chemical was not considered by the study authors to be mutagenic under the conditions of the test.

However, it is known that the test strains of the bacteria cannot perform endocytosis like human cells and the bacterial cell wall forms a barrier against simple diffusion. The uptake of particles by bacterial cells is likely to be less than human cells (ECHA 2013; Doak *et al* 20l2). The lack of particle uptake in bacterial cells may potentially lead to incorrect negative results (Pfuhler *et al* 2013). The SCCS also stated in the opinion on the toxicity of the nanoforms of silica that data from bacterial reverse mutation assay may have no value for the assessment of genotoxic potential for nano-size particles (SCCS 2015).

In vitro mammalian cell gene mutation test
An *in vitro* mammalian cell gene mutation test report on the notified chemical was submitted. The test was conducted using L5178Y mouse lymphoma cells. Neither cellular toxicity nor significant increase in mutant frequency was observed in the absence or presence of metabolic activation. Under the conditions of the test, the notified chemical was not considered by the study authors to be mutagenic when tested at the original concentration as in Bindzil CC 301. However, the test report provided did not include physical-chemical characterisation of the notified chemical during the test, especially the particle size.

Other considerations
Compared to large particles, nano-size particles generally have different toxicokinetic profiles and may be more readily absorbed by oral, dermal and inhalation routes. In particular, inhalation of ultrafine particulate matters has been correlated to a number of adverse human health effects, including increased incidence of cardiovascular / respiratory disease and increased oxidative damage (including DNA damage) within the lung (Kaewamatawong *et al* 2006, Chen *et al* 2008). Exposure to nano-size particles via oral or dermal route may also result in other

adverse effects (Nishimori *et al* 2009; So *et al* 2008). As the physical-chemical properties of nano-size particles including shape, size, surface modification may greatly influence the toxicity profiles (Gatoo *et al* 2014; Zhu *et al* 2013), the currently available data on the notified chemical are insufficient to derive hazard conclusions on specific end points such as acute and repeated dose toxicity via inhalation.

The manufactured notified chemical in nano-size may possibly contain residual surface reactive epoxide groups, which are known to have the potential to cause cancer and reproductive toxicity (US EPA 2010). However, the NMR spectroscopy conducted on Bindzil CC 301 indicated that the epoxide groups were not detectable in freeze-dried samples.

Health hazard classification
As limited toxicity data were provided, the notified chemical cannot be classified according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

6.3. Human Health Risk Characterisation
Based on the available information, the notified chemical may cause irritation effects to skin and eyes. The potential for the notified chemical as nano-size particles to be able to penetrate skin cannot be fully ruled out. There is currently insufficient information to fully determine the toxicity profile of the notified chemical.

6.3.1. Occupational Health and Safety

Reformulation
Reformulation workers may come into contact with to the notified chemical in nano-size at concentration < 50%. Inhalation exposure to the chemical is not expected unless aerosols are formed during the processes. Workers may mainly have potential for risk of irritation effects. Systemic effects may occur only if nano-size particles of the notified chemical are absorbed through the skin. However, the potential for dermal absorption of the notified chemical is considered to be limited due to the product types introduced (e.g. water dispersions with concentration of the notified chemical at < 50%). The use of engineering controls (such as enclosed/automated processes and local exhaust ventilation) and suitable PPE (capable of protecting workers from exposure to nano-size particles) is expected to minimise the exposure and hence reduce the risk.

End Use
During end-use, professional workers, including painters, cleaners and construction workers, may come into contact with the notified chemical in nano-size at up to < 25% concentration. Inhalation exposure to the chemical is not expected as no spray application will be used. Similar to reformulation workers, these workers may mainly be at risk of irritation effects caused by the notified chemical. The use of suitable PPE, capable of protecting workers from nano-size particles, is expected to minimise the exposure and hence reduce the risk.

Given the stated engineering controls and PPE in place to minimise worker exposure to the notified chemical, the risk to workers is not considered to be unreasonable under the assessed use patterns.

6.3.2. Public Health
The notified chemical is intended for use in industrial applications only. The public may come into contact with building or article surfaces treated with products containing the notified chemical. However, the notified chemical used in coating and construction products is expected to be trapped into inert matrices. Residuals of the notified chemical on cleaned hard surfaces are not expected to remain as nano-size particles once dried and result in significant exposure.

A proportion of the notified chemical in industrial cleaning products will potentially be released to the environment. However, the notified chemical is expected to interact with biological materials and undergo heteroaggregation in the environment to form micro-size materials after the release. The released chemical will also be further diluted in the environment. Therefore, public exposure to nano-size particles of the notified chemical after the environment release is not expected to be significant.

When used in the proposed manner, the risk to public health from the use of the notified chemical is not considered to be unreasonable.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be imported into Australia in products of Levasil CC series including Levasil CC 151, Levasil CC 301, Levasil CC 302 and Levasil CC 401 for reformulating into industrial coatings or construction products. The notified chemical will also be imported as a component of finished construction products or industrial cleaning products. No significant release of the notified chemical is expected from transportation and storage except in the unlikely events of accidental spills or leaks. The spills and leaks will be contained and collected for recycling where appropriate, or disposed of in accordance with the State, Territory and Federal regulations.

The notified chemical will be blended with other ingredients for reformulation into finished industrial coatings or construction products within an enclosed or isolated environment. Specifically, the notified chemical will be manually weighed or metered directly into a blending tank and mixed with other ingredients to form finished products. Reformulation equipment will be washed with water or solvent. Wastes containing the notified chemical generated during reformulation include equipment wash water or solvent, residues in empty containers and spilt materials. Empty import containers and wash water or solvent are expected to be recycled or disposed of through licensed waste management facilities.

No reformulation of cleaning products containing the notified chemical will occur in Australia.

RELEASE OF CHEMICAL FROM USE

Industrial coatings

The notified chemical will be used as a component of coatings for building surfaces such as walls, roofs, wood and brick. Professional workers are expected to apply the coatings with brushes and rollers. No significant environmental release is expected from the use of the coating products containing the notified chemical.

Industrial cleaning products

The notified chemical as a component of industrial cleaning products will be used for hard surface cleaning at hospitals, schools, hotels and is expected to be washed with solvent or water and released to the sewers.

Construction products

The construction products containing the notified chemical will be used to treat concrete floor surfaces. Once the surface dries, the notified chemical is expected to be irreversibly bound within an inert matrix.

Spills will be absorbed with absorbent material and subsequently disposed of to landfill or via appropriate waste management operating companies. Residues containing the notified chemicals in application equipment are expected to be rinsed into containers, recycled, or allowed to cure before disposal as solid wastes to landfill.

RELEASE OF CHEMICAL FROM DISPOSAL

The majority of the notified chemical in coating products will be cured within an inert matrix on the surface to which it is applied and is expected to be disposed of to landfill along with the substrates at the end of their useful life. In landfill, the notified chemical is expected to remain associated with the substrates to which it has been applied.

A small proportion of the notified chemical may remain in end-use containers once the products are used up. Wastes and residues of the notified chemical in empty containers are expected to be collected and disposed of through an approved waste management facility according to the State, Territory and Federal regulations.

7.1.2. Environmental Fate

A major proportion of the notified chemical is expected to share the fate of the articles to which it has been applied and be disposed of to landfill. The submitted study by the notifier has demonstrated that a significant proportion of the notified chemical may aggregate and/or agglomerate to micro-size range after being dried on the surface of the substrate and re-dispersed into water. In addition, a recent study has shown that leachate released into water from paint matrix made of nano-size colloidal surface-modified silica, contained the

particulate silicon (Si) in composites together with calcium (Ca) (Al-Kattan *et al* 2015). In landfill, the notified chemical bound to coated articles is not expected to be either bioavailable or bioaccumulative.

Aquatic exposure of the notified chemical is expected when it is used as a component of industrial cleaning products. The notifier has indicated that the notified chemical did not change particle size in 0.1% $CaCl_2$ solution within one week. Therefore, the notified chemical may remain in nano-size range in the aqueous phase under environmental conditions and may be released to the sewers in the size < 100 nm when used for hard surface cleaning. Published information on fate of other forms of colloidal silica nanoparticles suggests that surface functionalisation may significantly influence sedimentation processes in sewage treatment plants (STPs) (Walden *et al* 2016; Jarvie *et al* 2009). Significant proportion of the notified chemical may be removed due to nanoparticle heteroaggregation with suspended solids and via interaction with surface of microorganisms present in the activated sludge within STPs (Rottman *et al* 2012). The highest concentration of the notified chemical is expected to occur in landfill, soil, sludge and sediment compartments (Wang *et al* 2016). In these compartments the notified chemical is likely to accumulate and alter particle size, shape and surface chemistry. However, the notified chemical is not expected to bioaccumulate based on the currently available data (OECD 2016).

7.1.3. Predicted Environmental Concentration (PEC)

The calculation for the predicted environmental concentration (PEC) is summarised in the table below. Based on the reported use in cleaning products, it is assumed that 20% of the total import volume of the notified chemical is released to the sewer and there is no removal within STPs under a worst case scenario. The release is assumed to be nationwide over 260 working days per year.

Predicted Environmental Concentration (PEC) for the Aquatic Compartment		
Total Annual Import/Manufactured Volume	150,000	kg/year
Proportion expected to be released to sewer	20	%
Annual quantity of chemicals released to sewer	30,000	kg/year
Days per year where release occurs	260	days/year
Daily chemicals release	115.38	kg/day
Water use	200.0	L/person/day
Population of Australia (Millions)	24.386	million
Removal within STP	0	%
Daily effluent production	4,877	ML
Dilution Factor – River	1.0	
Dilution Factor – Ocean	10.0	
PEC – River:	23.66	µg/L
PEC – Ocean:	2.37	µg/L

STP effluent re-use for irrigation occurs throughout Australia. The agricultural irrigation application rate is assumed to be 1,000 L/m^2/year (10 ML/ha/year). The notified chemical in this volume is assumed to infiltrate and accumulate in the top 10 cm of soil (density 1,500 kg/m^3). Using these assumptions, irrigation with a concentration of 23.66 µg/L may potentially result in a soil concentration of approximately 157.7 µg/kg. Assuming accumulation of the notified chemical in soil for 5 and 10 years under repeated irrigation, the concentration of notified chemical in the applied soil in 5 and 10 years may be approximately 789 µg/kg and 1,577 µg/kg, respectively.

7.2. Environmental Effects Assessment

No ecotoxicological data were available for the notified chemical. Literature review indicates that different forms of nano-size silica exhibit different ecotoxicity depending on the size and surface chemistry of the nanoparticles. Read-across data indicate that silica-based nanomaterials may be harmful to aquatic life based on modified acute immobilisation test of *Daphnia magna* conducted on 14 nm fumed silica nanoparticles (72 h EC_{50} = 29.7 mg/L) (Clément *et al* 2013). However, the silica-based nanomaterials may exhibit very different physical-chemical properties depending on synthetic methods, sizes and surface modifications, and there might not be a strong scientific basis for grouping approach to use read-across methodology from available data on other forms of silica-based nanomaterials for hazard characterisation purposes.

However, if a large dataset for different taxonomic groups is available, probabilistic species sensitivity distributions (PSSD) may be used to derive a predicted no-effect concentrations (PNEC) and provide an estimate of the potentially affected fraction of species that will be harmed from exposure to silica-based nanomaterials (ECHA 2008). Wang *et al* (2016) have computed PSSD of silica-based nanomaterials in surface waters based on

20 ecotoxicological endpoints from 8 different species. A predicted no-effect concentration (PNEC) of 1,023 µg/L for the aquatic compartment was obtained by extracting the 5th percentile from the PSSD (Wang *et al* 2016). However, the computed PSSD is not specific to the notified chemical and covers a wide range of silica-based nanomaterials of different sizes with different surface modifications. In addition, there are uncertainties associated with measurements of effect concentrations for the tested aquatic organisms due to varied testing conditions as testing conditions have not been harmonised and standardised for nanomaterials.

7.3. Environmental Risk Assessment

The Risk Quotients (Q = PEC/PNEC) for discharge of treated effluents containing the notified chemical have not been calculated. However, the calculated PEC (23.66 µg/L) for the notified chemical is expected to be approximately one order of magnitude lower than PNEC (1,023 µg/L) derived from PSSD conducted on different forms of silica-based nanomaterials or PNEC (297 µg/L) derived from the most sensitive acute endpoint for *D. magna*. Additionally, the presence of natural organic matter in surface water may further decrease the toxicity of silica-based nanomaterials (Van Hoecke *et al* 2011). Therefore, the release of the notified chemical is not expected to lead to ecotoxicologically significant concentrations.

Based on the currently available information about the aquatic hazards of silica nanomaterials and assessed use pattern, the notified chemical in nano-size is not expected to pose an unreasonable risk to the environment. However, if additional hazard information becomes available to indicate that the notified chemical in nano-size has hazard characteristics of concern to the environment, then the risks will need to be re-assessed.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Partition Coefficient (n-octanol/water) log Pow < -3.2 at 20 °C

Method OECD TG 117 Partition Coefficient (n-octanol/water)

Remarks The partition coefficient was estimated based on the dispersibility in water and concentrations of the notified chemical in the n-octanol phase. The concentrations of the notified chemical were below detection limits in the n-octanol phase.

Generally, this test is not considered to be appropriate for nano-size materials as these materials cannot reach thermodynamic equilibrium by distribution between two phases.

Test Facility AkzoNobel (2014)

Particle Size 6.5 – 43.82 nm

Method A) Dynamic light scattering (DLS, Malvern Zetasizer) was used to determine the originally manufactured water dispersions.

B) A test was conducted to determine whether the notified chemical remains in nano-size after being applied as wet films onto substrates, dried and re-dispersed in water. The samples were applied onto clean glass plates and dried for 72 hours at room temperature. The dried films were scraped off, weighted, and re-dispersed in 20 mM NaCl. The dispersions were then filtered with 5 µm pore size syringe filters. Particle size distributions of the filtered fractions were measured by DLS while the size distributions of the coarse fractions were measured by laser diffraction.

A) Particle Size Distribution by Number in Originally Manufactured Water Dispersions:

Product	*Detected Size Range (nm)*	*Z-Average Size (nm)*
Bindzil CC 151	6.50 – 28.21	18.03
Bindzil CC 301	6.50 – 32.67	27.02
Bindzil CC 302	8.72 – 32.67	19.03
Bindzil CC 401	11.70 – 43.82	23.54

B) Particle Size Distribution by Volume for Dried (Aggregated) Chemical Re-Dispersed in Water:

Product	*Mean Diameter of Fresh Material (nm)*	*Mean Diameter of Particles in Filtered Fraction (nm)*	*Mass of Particles with size < 10 µm in Coarse Fraction (%)*
Bindzil CC 151	14.66	172.4	0.09
Bindzil CC 301	16.05	229.4	0.23
Bindzil CC 302	16.38	67.58	0.16
Bindzil CC 401	18.82	34.37	0.26

Remarks A) The originally manufactured notified chemical in water dispersions has typical particle size < 100 nm.

B) The results showed that, after drying process, less than 0.3% of the mass of re-dispersed notified chemical was present in the form of particles with size < 10 µm. Particles with size < 100 nm were detected in filtered fractions of the re-dispersed notified chemical.

Test Facility Malvern Instruments (2013a, b, c and d) and AkzoNobel (2015)

Flash Point

Bindzil CC 151	> 95 °C
Bindzil CC 301	61 °C
Bindzil CC 302	53 °C
Bindzil CC 401	61 °C

Method ASTM D93/A-07

Remarks Based on measured flash points:

Bindzil CC 151	Not a flammable liquid
Bindzil CC 301	Category 4 flammable liquid

	Bindzil CC 302	Category 3 flammable liquid
	Bindzil CC 401	Category 4 flammable liquid
Test Facility	Saybolt (2010)	

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – inhalation (Study 1)

TEST SUBSTANCE	Bindzil CC30 Ethanol-Based (Analogue chemical at ~ 30% concentration)
METHOD	OECD TG 403 Acute Inhalation Toxicity EC Council Regulation No 440/2008, 93/21/EEC B.2 Acute Toxicity (Inhalation)
Species/Strain	Rat/HanRcc:WIST(SPF)
Vehicle	Water
Method of Exposure	Nose-only exposure
Exposure Period	4 hours
Physical Form	Liquid aerosol
Particle Size	Mass median aerodynamic diameter (MMAD) = 3.02 µm with 59.1% of all aerosol particles < 4 µm
Remarks - Method	No significant deviations of protocol were noted. The test preparations were adjusted for dry silica contents.

RESULTS

Group	*Number and Sex of Animals*	*Dry Silica Concentration (mg/L)*		*Mortality*
		Nominal	*Actual*	
1	10 (5 M/5 F)	5.59	5.126	0/10

LC50	> 5.126 mg/L/4 hours
Signs of Toxicity	There were no spontaneous deaths. All animals were sacrificed as scheduled. Examination of each animal during and after exposure did not reveal any clinical signs during the 15-day observation period.
Effects in Organs	One female rat was found to have several dark red foci in the lungs.
Remarks - Results	In female rats, there was a slight retardation in body weight gain.
CONCLUSION	The analogue chemical was considered to be of low acute toxicity via inhalation under the conditions of the test.
TEST FACILITY	RCC (2007a)

B.2. Acute toxicity – inhalation (Study 2)

TEST SUBSTANCE	Bindzil CC30 Methanol-Free (Analogue chemical at ~ 30% concentration)
METHOD	OECD TG 403 Acute Inhalation Toxicity EC Council Regulation No 440/2008, 93/21/EEC B.2 Acute Toxicity (Inhalation)
Species/Strain	Rat/HanRcc:WIST(SPF)
Vehicle	Water
Method of Exposure	Nose-only exposure
Exposure Period	4 hours
Physical Form	Liquid aerosol
Particle Size	MMAD = 2.87µm with 61.6% of all aerosol particles < 4 µm
Remarks - Method	No significant deviations of protocol were noted. The test preparations were adjusted for dry silica contents.

RESULTS

Group	*Number and Sex of Animals*	*Dry Silica Concentration (mg/L)*		*Mortality*
		Nominal	*Actual*	
1	10 (5 M/5 F)	5.40	5.180	0/10

LC50	> 5.180 mg/L/4 hours
Signs of Toxicity	There were no spontaneous deaths. All animals were sacrificed as scheduled. Examination of each animal during and after exposure did not reveal any clinical signs during the 15-day observation period.
Effects in Organs	One female rat was found to have reddish discolouration in thymus.
Remarks - Results	Except for a slight body weight loss between Day 1 and Day 4 in one female, all animals showed normal body weight gain during the 15-day observation period.
CONCLUSION	The analogue chemical was considered to be of low acute toxicity via inhalation under the conditions of the test.
TEST FACILITY	RCC (2007b)

B.3. Skin absorption – *in vitro* method

TEST SUBSTANCE	Bindzil CC 301 (Notified chemical at < 50% concentration)
METHOD	OECD TG 428 Skin Absorption: *In Vitro* Method
Vehicle	None
Remarks - Method	The test substance was applied undiluted. The absorption and distribution of silica from the test substance was measured *in vitro* through human epidermis. The doses were applied to the skin surface at 10 µL/cm^2 and left unoccluded for an exposure period of 24 hours. Samples were analysed by Inductively Coupled Plasma Optical Emission Spectrophotometry. Untreated cells were included to measure the background silica levels within the test system. Particles size of the test substance was not determined at the time of testing.

RESULTS

Absorption into receptor fluid

Actual Dose	2,850	µg silica/cm^2
Number of Cells Used	5	cells
Absorption Rate	< 0.074*	µg/cm^2/hour
Amount absorbed	< 1.77*	µg/cm^2
Percentage Absorbed	< 0.062*	%

* Figures ≤ reporting limits, indicative of background level of silica

Silica mass balance

Test compartment	*Bindzil CC 301*		*Untreated control*[#]	
	µg silica/cm^2	*% silica recovered^*	*µg silica/cm^2*	*% silica recovered*
Donor chamber	37.3	1.31	16.1	14.25
Skin wash at 24 hours	2,920	102.46	78.0	69.03
Tape strips	90.6	3.18	15.8	13.98
Remaining epidermis	10.9	0.38	3.51	3.11
Receptor fluid	< 1.77*	< 0.06*	< 1.77*	< 1.57*
Total recovered	3,059	107.33	113	100.00

Background silica distribution ^ Compared to the dose applied (2,850 µg silica/cm^2)

* Figures ≤ reporting limits, indicative of background level of silica

Remarks - Results	The results showed that the absorption of silica contents from the test substance through human epidermis was slow and the majority of the applied dose was removed by skin washing after 24 hours. A small amount of silica was found within the untreated control and was considered to be

the background level.

CONCLUSION Dermal absorption of silica contents of the test substance was considered by the study authors to be negligible under the conditions of the test.

TEST FACILITY Dermal Technology Laboratory (2013)

B.4. Skin sensitisation – mouse local lymph node assay (LLNA)

TEST SUBSTANCE Bindzil CC 301 (Notified chemical at < 50% concentration)

METHOD OECD TG 429 Skin Sensitisation: Local Lymph Node Assay
EC Directive 2004/73/EC B.42 Skin Sensitisation (Local Lymph Node Assay)

Species/Strain	Mouse/CBA/J
Vehicle	*N,N*-Dimethyl formamide (DMF)
Preliminary study	Yes
Positive control	Positive control was not conducted in parallel with the test substance but had been conducted previously in the test laboratory using α-hexylcinnamaldehyde.
Remarks - Method	No significant deviations of protocol were noted.

RESULTS

Concentration (% w/w)	*Number and sex of animals*	*Proliferative response (DPM/lymph node)*	*Stimulation Index (SI) (Test/Control Ratio)*
Test Substance			
0 (vehicle control)	5 F	623	1.0
25	5 F	532	0.9
50	5 F	476	0.8
100	5 F	423	0.7
*Historical Positive Control**			
0 (vehicle control)	5 F	543	1.0
5	5 F	583	1.1
10	5 F	1696	3.1
25	5 F	1994	3.7

* α-Hexylcinnamaldehyde

Remarks - Results The test substance did not elicit a SI ≥ 3 when tested up to 100% concentration (with notified chemical at < 50% concentration).

CONCLUSION There was no evidence of induction of a lymphocyte proliferative response indicative of skin sensitisation to the notified chemical under the conditions of the test.

TEST FACILITY WIL Research (2015a)

B.5. Genotoxicity – bacteria

TEST SUBSTANCE Bindzil CC 301 (Notified chemical at < 50% concentration)

METHOD OECD TG 471 Bacterial Reverse Mutation Test
EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria
Plate incorporation procedure

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98 and TA100 *E. coli*: WP2uvrA	
Metabolic Activation System	Rat liver S9 fraction mix induced by Aroclor 1254	
Concentration Range in Main Test	With or without metabolic activation: Test 1	5.4 – 5,000 µg/plate

	Test 2 52 – 5,000 µg/plate
Vehicle	Water
Remarks - Method	No significant deviation of protocol was noted. The concentrations of the test preparations were adjusted for the notified chemical based on the concentration of the product. Particles size was not determined at the time of testing.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in*		
	Cytotoxicity in Test	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	> 5,000	> 5,000	Negative
Test 2	> 5,000	> 5,000	Negative
Present			
Test 1	> 5,000	> 5,000	Negative
Test 2	> 5,000	> 5,000	Negative

Remarks - Results	The notified chemical did not induce a significant dose-related increase in the number of revertant colonies in *S. typhimurium* and *E. coli* strains tested with or without metabolic activation. The negative and strain-specific positive controls indicated that the test conditions were adequate and the metabolic activation system functioned properly.
CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	WIL Research (2015c)

B.6. Genotoxicity – *in vitro*

TEST SUBSTANCE	Bindzil CC 301 (Notified chemical at < 50% concentration)
METHOD	OECD TG 476 *In vitro* Mammalian Cell Gene Mutation Test EC Directive 2000/32/EC B.17 Mutagenicity - *In vitro* Mammalian Cell Gene Mutation Test
Species/Strain	Mouse
Cell Type/Cell Line	Mouse lymphoma cells/L5178Y/TK$^{+/-}$-3.7 2C
Metabolic Activation System	Rat liver S9 fraction mix induced by phenobarbital and ß-naphthoflavone
Vehicle	RPMI 1640 (HEPES buffered) cell culture medium
Remarks - Method	No significant deviations of protocol were noted. The concentrations of the test preparations were adjusted for the notified chemical based on the concentration of the product. In a dose range finding test, no cytotoxicity was observed up to the highest concentration of 5,000 µg/mL with or without metabolic activation. Particle size was not determined at the time of testing.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	1.7, 5.4, 17, 52, 164, 512, 1,600 and 5,000	24 hours	2 days
Test 2	1.7, 5.4, 17, 52, 164, 512, 1,600 and 5,000	3 hours	2 days
Present			
Test 1	Not conducted	Not conducted	Not conducted
Test 2	1.7, 5.4, 17, 52, 164, 512, 1,600 and 5,000	3 hours	2 days

All cultures were selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in*		
	Cytotoxicity in Test	*Precipitation*	*Genotoxic Effect*
Absent			
Test 1	> 5,000	> 5,000	Negative
Test 2	> 5,000	> 5,000	Negative
Present			
Test 1	Not conducted	Not conducted	Not conducted
Test 2	> 5,000	> 5,000	Negative

Remarks - Results

The test conditions were confirmed as appropriate using positive controls. In the absence or presence of metabolic activation, the notified chemical did not induce a significant increase in the mutation frequency under the test conditions.

CONCLUSION

The notified chemical was not clastogenic to mouse lymphoma cells treated *in vitro* under the conditions of the test.

TEST FACILITY

WIL Research (2015b)

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