Australian Government

Australian Pesticides and Veterinary Medicines Authority

PUBLIC RELEASE SUMMARY

on the evaluation of the new active *Bacillus amyloliquefaciens* MBI 600 in the product Serifel Biofungicide

APVMA Product Number 82600

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PREFACE

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the Australian Government regulator responsible for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia. Before approving an active constituent and/or registering a product, the APVMA must be satisfied that the statutory criteria, including the safety, efficacy, trade and labelling criteria, have been met. The information and technical data required by the APVMA to assess the statutory criteria of new chemical products, and the methods of assessment, must be consistent with accepted scientific principles and processes. Details are outlined on the APVMA website.

The APVMA has a policy of encouraging transparency in its activities and seeking community involvement in decision making. Part of that process is the publication of Public Release Summaries for products containing new active constituents. This Public Release Summary is intended as a brief overview of the assessment that has been conducted by the APVMA and of the specialist advice received from advisory agencies, including other Australian Government agencies and State departments of primary industries. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience to encourage public comment.

About this document

This is a Public Release Summary.

It indicates that the APVMA is considering an application for registration of an agricultural or veterinary chemical. It provides a summary of the APVMA's assessment, which may include details of:

- the toxicology of both the active constituent and product
- the residues and trade assessment
- occupational exposure aspects
- environmental fate, toxicity, potential exposure and hazard
- efficacy and target crop or animal safety.

Comment is sought from interested stakeholders on the information contained within this document.

Making a submission

In accordance with sections 12 and 13 of the Agvet Code, the APVMA invites any person to submit a relevant written submission as to whether the application for registration of the active *Bacillus amyloliquefaciens* MBI 600 and the product Serifel Biofungicide should be granted. Submissions should relate only to matters that the APVMA is required, by legislation, to take into account in deciding whether to grant the application. These matters include aspects of public health, occupational health and safety, chemistry and manufacture, residues in food, environmental safety, trade, and efficacy and target crop or animal safety. Submissions should state the grounds on which they are based. Comments received that address issues outside the relevant matters cannot be considered by the APVMA.

Submissions must be received by the APVMA by close of business on 12 February 2019 and be directed to the contact listed below. All submissions to the APVMA will be acknowledged in writing via email or by post.

Relevant comments will be taken into account by the APVMA in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling.

When making a submission please include:

- contact name
- company or group name (if relevant)
- email or postal address (if available)
- the date you made the submission.

All personal information, and confidential information judged by the APVMA to be confidential commercial information (CCI)[1] contained in submissions will be treated confidentially. Unless requested by the submitter, the APVMA may release a submission, with any CCI redacted, to the applicant for comment.

Written submissions on the APVMA's proposal to grant the application for registration that relate to the grounds for registration should be addressed in writing to:

Case Management and Administration Unit
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Kingston ACT 2604

Phone: +61 2 6210 4701
Fax: +61 2 6210 4721
Email: enquiries@apvma.gov.au

Further information

Further information can be obtained via the contact details provided above.

Copies of technical evaluation reports covering chemistry, efficacy and safety, toxicology, occupational health and safety aspects, residues in food and environmental aspects are available from the APVMA on request.

Further information on Public Release Summaries can be found on the APVMA website.

[1] A full definition of 'confidential commercial information' is contained in the Agvet Code.

1 INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of Serifel Biofungicide, and approval of the new active constituent, *Bacillus amyloliquefaciens* MBI 600.

1.1 Applicant

BASF Australia Ltd.

1.2 Purpose of application

BASF Australia Ltd has applied to the APVMA for registration of the new product Serifel Biofungicide, containing 110 g/kg (>5.5 x 10^{10} colony forming units [CFU]/g), as a wettable powder formulation of the new active constituent *B. amyloliquefaciens* MBI 600.

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of the product Serifel Biofungicide, and approval of the new active constituent *B. amyloliquefaciens* MBI 600.

1.3 Proposed claims and use pattern

Serifel Biofungicide is a biological fungicide intended for use as a preventative treatment in the control of Botrytis bunch rot in grapevines and Grey mould in strawberries, both caused by the pathogen Botrytis cinerea. It is applied at a rate of 50–75 g/100 L in grapevines and 500 g/ha in strawberries, with applications made at multiple time points in fruit development.

1.4 Mode of action

The bacterium, *B. amyloliquefaciens*, is prevalent in soils and has been found in a variety of habitats worldwide. The MBI 600 strain of *B. amyloliquefaciens* is antagonistic to fungal plant pathogens. This antagonism may be achieved in several ways including nutrient competition, site exclusion, colonisation, and attachment of the bacteria to the fungal pathogen.

The Fungicide Resistance Action Committee (FRAC), has designated *B. amyloliquefaciens* MBI 600 (synonym *B. subtilis* MBI 600) as a Group 44 fungicide, this mode of action is defined as a microbial disrupter of pathogen cell membranes.

1.5 Overseas registrations

The active constituent *B. amyloliquefaciens* MBI 600 was first registered with the United States Environmental Protection Agency (US EPA) as *B. subtilis* strain MBI 600.

Serifel Biofungicide, containing the active constituent *B. amyloliquefaciens* MBI 600 is currently registered under the names:

- Serifel in Bolivia, Canada, France, Greece, Italy, Mexico, Peru, Poland, Portugal, Spain, Thailand, Turkey, and the USA
- Serifel 10 WP in Costa Rica, Dominican Republic, El Salvador, Guatemala, Honduras, and Nicaragua
- Serifel WP in Malaysia
- Subtilex in New Zealand
- Subtilex NG Biological Fungicide in the USA
- Duravel in Brazil
- Toreda in the Netherlands.

2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

The active constituent *B. amyloliquefaciens* MBI 600 is manufactured overseas. Details of the chemical name, structure, and physicochemical properties of *B. amyloliquefaciens* MBI 600 are listed below (Tables 1–2). *B. amyloliquefaciens* MBI 600 is an aerobic, endospore-forming bacillus, originating from an indigenous wild type isolated from leaves of broad bean plants (*Vicia faba*). The occurrence of *B. amyloliquefaciens* is abundant in any environmental media, predominantly in soil. The organism is an ellipsoidal rod shaped bacterium, 0.7—0.8 µm in width by 2–3 µm in length.

Table 1: Key identification information and characteristics for *Bacillus amyloliquefaciens* strain MBI 600

COMMON NAME:	*Bacillus amyloliquefaciens* MBI 600
SCIENTIFIC CLASSIFICATION:	Kingdom: Bacteria Phylum: Firmicutes Class: Bacilli Order: Bacillales Family: Bacillaceae Genus: *Bacillus* Species: *Bacillus amyloliquefaciens*
PRODUCT NAME:	Serifel Biofungicide
ACCESSION NUMBER:	NCIMB 12376
MICROBIAL IMPURITIES:	*Salmonella*: absent in a 25 gram sample Yeasts and moulds: <1000 CFU/g *Escherichia coli*: absent in a 1 gram sample *Staphylococcus aureus*: absent in a 1 gram sample
SPORE COUNT:	Not less than 5.0×10^{11} CFU/g

2.2 Formulated product

The product Serifel Biofungicide will be manufactured in Australia and overseas. Tables 3 and 4 outline some key aspects of the formulation and physicochemical properties of the product.

The product *Serifel Biofungicide* is a wettable powder (WP) formulation containing *B. amyloliquefaciens* MBI 600 with not less than 5.5×10^{10} CFU/g of viable spores. The appearance of the product is that of a light brown free-flowing homogeneous powder with a faint yeasty odour. It is not explosive, has no oxidising properties and is not flammable. It has slightly alkaline pH value around 8 for a 1% dilution. It will be available in 50 g, 500 g, 1 kg, 2 kg, 2.5 kg, 5 kg, 10 kg, and 20 kg re-sealable plastic-covered foil pouches and high density polyethylene (HDPE) bottles, with multi-packs of 2, 4, 5 or 10 500 g foil pouches or HDPE bottles also proposed.

Table 2: Key aspects of the formulation of the product Serifel Biofungicide

DISTINGUISHING NAME:	Serifel Biofungicide
FORMULATION TYPE:	Wettable powder (WP)
ACTIVE CONSTITUENT CONCENTRATION/S:	110 g/kg *Bacillus amyloliquefaciens* MBI 600, giving >5.5 x 10^{10} CFU/gram

Table 3: Physicochemical properties of the product Serifel Biofungicide

PHYSICAL FORM:	Light brown free-flowing homogeneous powder
PH:	A 1% aqueous suspension is pH 8.7 at 22°C
SPECIFIC GRAVITY / DENSITY:	1.04 g/mL
SAFETY PROPERTIES:	Not flammable. No flash point. No oxidising or explosive properties
STORAGE STABILITY:	Stable for at least 34 months under normal conditions

2.3 Recommendations

The APVMA Chemistry section has evaluated the chemistry of the active constituent *B. amyloliquefaciens* MBI 600 and associated product Serifel Biofungicide, including the manufacturing process, quality control procedures, stability, batch analysis results and analytical methods, and found them to be acceptable. The available storage stability data indicate that the formulated product is expected to remain stable for at least 34 months when stored below 25°C.

As with other biological active constituents, it is not proposed to establish a standard for *B. amyloliquefaciens* MBI 600.

Based on a review of the chemistry and manufacturing details, the registration of Serifel Biofungicide, and approval of the active constituent *B. amyloliquefaciens* MBI 600, are supported from a chemistry perspective.

3 TOXICOLOGICAL ASSESSMENT

3.1 Evaluation of toxicology

The toxicological data for *B. amyloliquefaciens* MBI 600 is considered sufficient to determine its toxicology profile and to characterise the risk to humans.

The toxicological data evaluated consisted of acute toxicity studies conducted in laboratory animals with *B. amyloliquefaciens* MBI 600; in vitro genotoxicity tests conducted with B. amyloliquefaciens MBI 600; acute toxicity, infectivity and pathogenicity studies conducted in laboratory animals with a formulation (containing ≥5.5 x 10^{10} viable spores of *B. amyloliquefaciens* MBI 600/g) comparable to the product Serifel Biofungicide; published regulatory reports from other jurisdictions dealing with *B. amyloliquefaciens* and related strains (European Food Safety Authority, EFSA, and US EPA); and a range of clinically relevant publications.

In interpreting the data, it should be noted that toxicity tests conducted in laboratory animals generally use doses that are high compared with likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. Findings of adverse effects in any one species do not necessarily indicate that such effects might be generated in humans. From a conservative risk assessment perspective however, adverse findings in animal species are assumed to represent potential effects in humans, unless convincing evidence of species specificity is available. Where possible, considerations of the species-specific mechanisms of adverse reactions weigh heavily in the extrapolation of animal data to likely human hazard. Equally, consideration of the risks to human health must take into account the likely human exposure levels compared with those, usually many times higher, which produce effects in animal studies. Toxicity tests should also indicate dose levels at which the specific toxic effects are unlikely to occur.

Pharmacokinetics

No pharmacokinetic studies were available for *B. amyloliquefaciens* MBI 600. *B. amyloliquefaciens*, is an environmental organism, commonly and normally present on fruit and vegetables. Ingested organisms from residues on treated produce will be subject to the normal digestive and immune surveillance mechanisms applicable to any ingested organism, and to the naturally occurring load of this organism on fruits and vegetables. The organism does not produce toxins or antimicrobial compounds under the culture conditions used for production.

Acute toxicity (active)

The acute toxicity of *B. amyloliquefaciens* MBI 600 was low, with no treatment related mortalities following oral, dermal and inhalational administration (LD_{50} >5000 mg/kg bw, LD_{50} >5050 mg/kg bw and LC_{50} >5320 mg/m^3/4 h, respectively). *B. amyloliquefaciens* MBI 600 was a slight eye irritant but not a skin irritant. *B. amyloliquefaciens* MBI 600 was found to be a skin sensitiser in a Guinea pig maximisation test where induction included intradermal injection of the test substance. However, this result is unlikely to occur in agricultural occupational settings, as the microorganism is unable to penetrate the skin barrier.

There was no evidence of pathogenicity or infectivity following intra-tracheal inoculation (1 x 10^8 viable spores/rat), or intravenous administration (>1 x 10^7 viable spores/rat) of *B. amyloliquefaciens* MBI 600. No mortalities were observed in any of the acute toxicity studies.

Acute toxicity (product)

The acute toxicity of the product, Serifel Biofungicide, containing 110 g/kg (>5.5 x 10^{10} CFU/g) *B. amyloliquefaciens* MBI 600 in a wettable powder formulation, was based on the assessment of studies conducted with the formulated product, or in the case of the skin sensitisation studies, with a similar formulation containing an equivalent concentration of *B. amyloliquefaciens* MBI 600 spores. The acute toxicity profile of the formulated product was low by oral, dermal and inhalational routes of administration. The formulated product was not irritating or sensitising to the skin but it was a slight eye irritant.

Repeat-dose toxicity

Repeat dose toxicity studies were not conducted, as there was an absence of adverse findings in the acute toxicology and infectivity/pathogenicity studies. This was considered reasonable and appropriate for a non-pathogenic biological active constituent of this type. Reproductive toxicity, developmental toxicity and neurotoxicity studies have also not been performed with *B. amyloliquefaciens* MBI 600, which was also considered reasonable and appropriate given the acute toxicity profile.

Genotoxicity

The genotoxicity potential was investigated *in vitro* in a standard Ames test using the guideline range of bacterial strains. All *in vitro* outcomes in the study were negative. Considering the results of this study and supportive evidence of negative genotoxic potential from overseas regulatory agencies reports on related substrains of *B. amyloliquefaciens* (US EPA, 1997; EFSA, 2008; 2013), *B. amyloliquefaciens* MBI 600 was considered unlikely to possess genotoxic potential.

Reports related to human toxicity

A review of available clinically relevant publications related to *B. amyloliquefaciens* was conducted, which concurred with the outcome of a review of the safety concerns for the Qualified Presumption of Safety (QPS) status of biological agents that are added intentionally to food and animal feeds including *Bacillus* species which was conducted by the European Food Safety Authority (EFSA 2013). Briefly, there was no substantive evidence that *B. amyloliquefaciens* was the causative agent in the clinical reports investigated. The EFSA report also confirmed the non-toxigenic/non-pathogenic potential of *B. amyloliquefaciens* towards humans. However, as noted in both the EFSA (2013) and US EPA (1997) reports, the review found that respiratory mediated allergenic response developing in sensitive individuals following exposure to *B. amyloliquefaciens* MBI 600 could not be excluded.

Microbiological properties

B. amyloliquefaciens is a ubiquitous bacterium found in water, soil, air, decomposing plant material, and on fresh produce. Densities of *B. amyloliquefaciens* in indoor air and settled dust of schools and day-care centres have been reported at around 10-100 CFU/g.

Bacillus bacteria are mainly Gram-positive but may stain variably. They are rod-shaped cells with rounded or squared ends ranging in size from 0.5 x 1.2 to 2.5 x 10 µm.

B. amyloliquefaciens has been used as a probiotic in broiler feed, to produce proteolytic enzymes for laundry detergents, and to produce a range of enzymes such chitinase, protease and lipases which suppress fungi and nematode viability. Members of the *B. subtilis* complex (which includes *B. amyloliquefaciens*) produce secondary metabolites in uncontrolled growing conditions, and some of these metabolites have antimicrobial and haemolytic properties.

3.2 Health-based guidance values and poisons scheduling

Poisons Standard

On 10 April 2018 the Delegate of the Secretary of the Department of Health published a final Scheduling decision to amend the existing Appendix B entry for *Bacillus amyloliquefaciens*, strain QST 713 to remove ‘strain QST 713’; thereby creating a group entry for all *Bacillus amyloliquefaciens* strains and capturing both strain QST 713 and MBI 600. The reason for the Delegate’s decision was the low toxicity of *Bacillus amyloliquefaciens.* Furthermore the scheduling history of *B. amyloliquefaciens* described the organism as being of very low infectivity and low pathogenicity, and presenting a low risk of causing skin irritancy. This decision was implemented on 1 June 2018.

Health-based guidance values

The Acceptable Daily Intake (ADI) is that quantity of a compound that can safely be consumed on a daily basis for a lifetime. The Acute Reference Dose (ARfD) is the maximum quantity of a compound that can safely be consumed over a short period of time, usually in one meal or during one day. As *B. amyloliquefaciens* (including strain MBI 600) is a naturally occurring organism, residues from its use are unlikely to be distinguishable from naturally occurring background levels of the organism. Furthermore, *B. amyloliquefaciens* was not infective or pathogenic and has low toxicity. For these reasons, establishing health based-guidance values (ADI and ARfD) was unnecessary.

3.3 Recommendations

The APVMA has evaluated the toxicological aspects of the active constituent *B. amyloliquefaciens* and the associated product Serifel Biofungicide, including the acute and chronic toxicity, genotoxicity, microbial pathogenicity, and human medical case reports, and found them to be acceptable. As the Scheduling Delegate of the Department of Health has included the active in appendix B of the Standard for Uniform Scheduling of Medicines and Poisons, no signal headings on the product label are necessary.

Based on a review of the toxicology of the active and associated product, registration of the active constituent B. amyloliquefaciens MBI 600 and the associated product Serifel Biofungicide are supported from a toxicological perspective.

4 RESIDUES ASSESSMENT

4.1 Metabolism

No metabolism studies are available for *B. amyloliquefaciens* MBI 600 in target plants or animals. However *B. amyloliquefaciens* MBI 600 is a naturally occurring organism which does not produce a mammalian toxin or toxic metabolite. No kinetics and metabolism data are required for this microbial product.

4.2 Residues in food and animal feeds

B. amyloliquefaciens MBI 600 is a wild type strain that has not been modified in any way and is ubiquitous in the receiving environment, including in water, soil, air, decomposing plant material and fresh produce. The expression of metabolites under the proposed conditions of use will be no different to the situations that exists naturally. It would not be possible to differentiate residues from natural sources from those arising from the proposed uses on the label.

The APVMA toxicology evaluation concluded that *B. amyloliquefaciens* is a common environmental organism likely to be present on fruit and vegetables. The organism is not infective or pathogenic and was not toxic at limit doses in acute toxicity tests, consequently the establishment of an Acceptable Daily Intake (ADI), or of an Acute Reference Dose (ARfD), is not required.

In the USA, an exemption from the requirement of a tolerance is established for residues of the biofungicide *B. amyloliquefaciens* MBI 600 (antecedent *B. subtilis* MBI 600) in or on all food commodities. In the EU no maximum residue levels (MRLs) are required for *B. amyloliquefaciens* MBI 600.

Currently in Australia a Table 5 entry in the MRL standard is established for the related strain *B. subtilis* strain QST 713 (*B. amyloliquefaciens*) when used as a fungicide on food producing crops.

Given the ubiquity of the bacterium in the soil and other environmental compartments and the lack of any identified toxicological hazard (as confirmed by the toxicology assessment), the proposed use of *B. amyloliquefaciens* MBI 600 in grapes and strawberries for control of *Botrytis cinerea* is not expected to pose a risk to the health of people consuming treated grapes or strawberries. A Table 5 entry in the MRL Standard is appropriate to cover the proposed use on grapes and strawberries.

4.3 Residues in animal commodities

Grape pomace from wine or juice production from treated crops may be fed to livestock. Treated vineyards may also be grazed by cattle or sheep.

It is noted that there is already a Table 5 entry for *Bacillus subtilis* for use as a direct fed microbial in animals. Feeding of treated pomace or grazing of treated vineyards by livestock is therefore not expected to be an issue from a residues perspective.

4.4 Dietary risk assessment

The toxicological assessment concluded that health based guidance values (ADI and ARfD) were not necessary. It is therefore not necessary to undertake a dietary risk assessment and a Table 5 entry to the MRL Standard has been recommended to cover the proposed use.

4.5 Recommendations

The following amendments are required to be made to the APVMA MRL Standard (Table 5).

Table 4: Amendments to the APVMA MRL Standard

AMENDMENTS TO TABLE 5	
SUBSTANCE	**USE**
ADD:	
***Bacillus subtilis* strain MBI 600 (*Bacillus amyloliquefaciens*)**	• When used as a fungicide on food producing crops

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Grapes (including dried grapes) and wine in addition to animal commodities are major export commodities. Because *B. amyloliquefaciens* is ubiquitous in the environment any residues as a result of the proposed use would be indistinguishable from naturally occurring levels. As a result there is not expected to be any risk to trade of grapes, wine or animal commodities.

6 WORK HEALTH AND SAFETY ASSESSMENT

Farmers, agricultural workers and professional spray operators will be the main users of Serifel Biofungicide. Workers may be exposed to the product including its active constituent, *B. amyloliquefaciens* MBI 600, when opening containers, mixing/loading, applying the spray mixture, maintaining equipment, cleaning up spills and equipment, and when performing work activities in treated crops. The main route of exposure to the product and active will be the skin, although exposure *via* inhalation and eye contact is also possible.

Serifel Biofungicide is considered to have low acute toxicity by oral, dermal and inhalational routes of exposure, it was not irritating or sensitising to the skin but it was a slight eye irritant. Based on the use pattern and this acute hazard profile, precautionary statements displayed on the product label are considered adequate to mitigate the risks for workers handling and preparing the product.

The toxicological assessment considered that it was possible that sensitive individuals repeatedly exposed to *B. amyloliquefaciens* MBI 600, may develop a respiratory mediated allergenic response. It is proposed that this risk can be minimised by including adequate precautionary statements and directions for workers handling the product to wear specified personal protective equipment (PPE) on the label.

The risks posed by use of the product to the public, and to workers re-entering treated crops was considered negligible and unlikely to be distinguishable from the risk posed by exposure to the naturally occurring organism.

6.1 Health hazards

Acute toxicological hazards of the product

Serifel Biofungicide was of low acute oral, dermal and inhalational toxicity, it was not irritating or sensitising to the skin but it was a slight eye irritant.

Based on this hazard profile, workers handling the product are at risk of slight eye irritation. This risk is adequately mitigated by displaying corresponding precautionary safety directions on the product label.

Repeat-dose hazards of the active, *B. amyloliquefaciens* MBI 600

The toxicological assessment considered possible that sensitive individuals repeatedly exposed to *B. amyloliquefaciens* MBI 600 may develop a respiratory mediated allergenic response.

This risk can be minimised by including adequate precautionary statements and directions for workers handling the product to wear specified personal protective equipment (PPE) on the label.

6.2 Occupational exposure

Exposure during use

Farmers, agricultural workers and professional spray applicators will be the main users of Serifel Biofungicide. Workers may be exposed to the product when opening containers; pouring, diluting or mixing the product; and cleaning up spills and equipment. Exposure to *B. amyloliquefaciens* MBI 600 in the finished spray mixture may also occur during loading, application and equipment clean-up or maintenance.

Exposure to the product was considered to be primarily *via* the dermal route during mixing/loading and application activities. Occupational exposure *via* the inhalational route was also considered to be likely. The pattern of exposure was considered to be long-term, based on the label statements of multiple applications throughout the year as part of a preventative fungicide program.

Exposure during re-entry or rehandling

The risk associated with re-entering treated areas is expected to be limited to exposure *via* the dermal route; exposure to dried spray may occur with activities such as the inspection of treated plants.

Given that no long-term adverse effects from ingestion or contact were anticipated with the microbial preparation, a quantitative risk assessment of post-application exposure was not considered necessary. The risk to workers re-entering treated crops was considered to be low, and therefore no-entry interval was considered necessary.

6.3 Public exposure

Public exposure to *B. amyloliquefaciens* resulting from the use of the product is unlikely to be distinguishable from naturally occurring background levels of this naturally occurring organism. Furthermore, *B. amyloliquefaciens* was not infective or pathogenic and has low toxicity.

6.4 Recommendations

The following first aid instructions, safety directions and precautionary (warning) statements are recommended for the product label.

First aid instructions

First aid is not generally required. If in doubt, contact a Poisons Information Centre (*eg* phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor.

Safety directions

Harmful if inhaled. Will irritate the eyes. Repeated exposure may cause allergic disorders. Do not inhale dust or spray mist. Avoid contact with the eyes. When opening the container and preparing the spray wear cotton overalls buttoned to the neck and wrist, a washable hat, a disposable dust face mask covering mouth and nose and disposable gloves. If product in eyes, wash it out immediately with water. Wash hands after use. After each day's use wash contaminated clothing.

The registration of Serifel Biofungicide, containing 110 g/kg (>5.5 x 10^{10} CFU/g) *B. amyloliquefaciens* MBI 600 in a wettable powder formulation, for the preventative control of various fungal diseases in grapevines and strawberries as proposed is supported. The product can be used safely if handled in accordance with the above first aid instructions and safety directions on the product label.

7 ENVIRONMENTAL ASSESSMENT

B. amyloliquefaciens is a non-pathogenic bacterium usually found in soils and on plant foliage. It is closely related to *B. subtilis*, a well-known soil bacterium of the *Bacillus* genus. The proposed label application rate of Serifel Biofungicide is 50–75 g/100 L of water for grapevines and 500 g/ha for strawberries, with a maximum of 5 kg/ha per season, and a maximum of ten applications per season. Environmental fate and effects studies were provided in support of the application.

7.1 Fate and behaviour in the environment

The fate and behaviour of *B. amyloliquefaciens* in the environment will be dependent upon a range of factors, including competition with other microorganisms (parasites/predators of fungi), soil parameters (pH, moisture, clay content) and agricultural practices such as tillage.

The predicted environmental concentrations of the bacterium in soil and water after a single foliar application of 500 g/ha were calculated to be 5.7×10^7 CFU/kg and 2.8×10^7 CFU/L, and after ten applications (assuming no growth or decline) 5.7×10^8 CFU/kg and 2.8×10^8 CFU/L. These figures were calculated assuming that the bacterial strain does not occur at background levels in the Australian environment.

Fate studies predict that any elevated level of *B. amyloliquefaciens* in soil following field will likely decline within a few days to approximately 102–104 CFU/g, this likely being due to competition/predation by other microorganisms and/or access to resources. The bacterium could be potentially spread by the movement of surface water, particularly rainfall, floods, spray drift and run-off. However, water is not regarded as being optimal for its survival, and levels are likely to be negligible after only a few days, whether at the point of application or at a distant location where it has been carried by one of the above mechanisms. Endospores of the bacterium may be dispersed by wind currents at distances of over 200 m, but survival in air will be reduced by exposure to UV light.

7.2 Effects and associated risks to non-target species

Biological pesticides can have direct and indirect adverse effects on non-target organisms, primarily through the production of toxic secondary metabolites and/or pathogenesis.

The mode of action for suppression of *Botrytis cinerea* by *B. amyloliquefaciens* MBI 600 is not well defined, but is understood to include the production of bioactive metabolites and competition for nutrients and space with the pathogen when both are present on a plant surface. Metabolites with potential antagonistic properties include the toxin amylosin and the cyclic lipopeptides surfactins, iturins, and fengycins.

The risk assessment evaluated the potential for adverse effects to non-target organisms.

Terrestrial vertebrates

The environmental effects submission included one study with rats and one with birds. The oral study with rats indicates that *B. amyloliquefaciens* MBI 600 is not toxic to these animals at 7.3 x 10^8 CFU/kg BW, and not pathogenic. The oral study with birds (Bobwhite quail) likewise indicates that the microorganism is non-toxic and non-pathogenic, with a NOEL of 6 x 10^{11} CFU/kg BW and a concentration leading to 50 % mortality (LD50) > 6 x 10^{11} CFU/kg BW. Mammalian studies also indicated a negligible risk. On the basis of US EPA toxicity rankings, the endpoints classify the bacterium as 'practically non-toxic' to mammals and birds. No reference could be found in submitted studies or publicly available literature recording *B. amyloliquefaciens* as pathogenic towards these organisms. The risk to mammals and birds is considered to be acceptable.

Aquatic species

Five aquatic organism effects studies for *B. amyloliquefaciens* MBI 600 were submitted by the applicant: (i) a 96 hour acute toxicity test with rainbow trout ; (ii) a 30 day toxicity study with carp; (iii) a 48 hour acute toxicity study with *Daphnia*; (iv) a 21 day *Daphnia* reproductive study; (v) 72 hour algal inhibition test.

No mortalities were recorded in the rainbow trout and carp studies, the NOECs for the microorganism in the respective studies being 9.97 x 10^{10} CFU/L and 2 x 10^{11} CFU/L. The acute toxicity study of *Daphnia* demonstrated a 10% reduction in mobility of the test animals in the presence of 1.9 x 10^{10} CFU/L of the microorganism, and an EC50 > 1.9 x 10^{10} CFU/L (100 mg/L). In the *Daphnia* reproductive study, a NOEC of 2 x 10^8 CFU/L was recorded for reproduction and a NOEC for adult mortality of 2.7 x 10^{10} CFU/L. A dose response relationship was observed in algae at very high concentrations, with an EC50 > 100 mg/L (> 5.8 x 10^8 CFU/L). Using the NOEC value of 2 x 10^8 CFU/L, a RQ value of 0.14 was calculated, this being less than one, indicating an acceptable risk at the screening level. In addition to the submitted data, consultation of publicly available literature found no report of pathogenicity or toxicity of *B. amyloliquefaciens* (and *B. subtilis*) towards aquatic organisms. The risk to aquatic organisms is considered to be acceptable.

Bees and other non-target arthropods

A 48 hour acute contact toxicity test on honeybees recorded percent mortality in the negative control, inactive test substance, and active test substance as 0%, 5.0 % and 3.3%, respectively. The positive controls demonstrated increased mortality with increased dose. The LD50 at 48 hrs was > 100 µg/bee (4.4 x 10^8 CFU/bee). On the basis of the US EPA toxicity rankings, the active constituents are 'practically non-toxic' to bees. A 20 day oral toxicity study gave an LD50 > 1.4 x10^7 CFU/bee (17.5 µg/bee). Assuming substantial decline in the numbers of the microorganism between applications, and a worse case exposure rate of 1.125 kg/ha, acute contact and acute oral toxicity risk quotient (RQ) values were calculated as ≤ 0.03 and ≤ 1.8, respectively. No reference could be found in submitted studies or publicly available literature *recording B. amyloliquefaciens* as toxic or pathogenic towards bees. Considering the lack of toxic or pathogenic effects at environmentally relevant rates, the risk to bees is considered to be acceptable.

Studies were submitted on the effects of *B. amyloliquefaciens* MBI 600 on a predatory coleopteran beetle, a predatory neuropteran (green lacewing), a predatory mite and silkworm larvae. These studies indicate that adverse effects on the beetle, the green lacewing and silkworm larvae are negligible at rates over 10× environmentally relevant rates. The LR50 values were determined to be > 1×10^9 CFU/ml. Arthropods are prone to infection by a range of microbial pathogens, including bacteria. Neither *B. subtilis* nor *B. amyloliquefacien*s is regarded as an entomopathogen. Any effects on other arthropods are expected to be minimal and transient. The risk to arthropods is considered to be acceptable.

Soil organisms

In a 56 day chronic toxicity, a NOEC > 2.9 x 10^9 CFU/g soil was determine for earthworms. No signs of toxicity, infectiveness or pathogenicity were observed. Earthworms appear to be extremely resistant to pathogens, there being no recorded microbial pathogen of these organisms that has detrimental effects on their growth and survival. The risk to earthworms is considered to be acceptable.

One submitted study included information on the effects to soil microorganisms of the application of *B. amyloliquefaciens* MBI 600. It was found that over a 30 day period the addition of this bacterium to soil had negligible effects on the levels of indigenous microorganisms (bacteria, fungi). Although the product is a fungicide, and despite the findings of the above study may have at least some activity against fungi other than the target (*Botrytis cinerea*), it is unlikely that any adverse effect on fungi will lead to a significant indirect adverse effect upon other aspects of an ecosystem, including non-target organisms of other taxa (eg plants, higher animals) that may be dependent upon microorganisms for food. The risk to microorganisms is considered to be acceptable.

Non-target terrestrial plants

No ecotoxicity studies were submitted on plants. Both *B. amyloliquefaciens* and *B. subtilis*, which as soil bacteria would be expected to have contact with plants, have never been classified as phytopathogens. In this context, no adverse effects upon plants are expected. The risk to terrestrial plants is considered to be acceptable.

7.3 Recommendations

This environmental risk assessment was conducted based on the submitted data and consultation of publicly available literature. The assessment has concluded that the risks of the active constituent to terrestrial vertebrates, invertebrates, microorganisms and plants, and aquatic organisms, are acceptable. The APVMA is unaware of any report of a significant adverse effect on a non-target organism by any strain of *B. amyloliquefaciens* or *B. subtilis* that has been used as a biological control agent. Consequently, the APVMA is satisfied that the proposed use of this product is unlikely to have an unintended effect that is harmful to animals, plants or things or the environment.

8 EFFICACY AND SAFETY ASSESSMENT

8.1 Proposed product use pattern

Serifel Biofungicide is a biological fungicide intended for use as a preventative treatment for *Botrytis* bunch rot in grapevines and grey mould in strawberries, both caused by the pathogen *Botrytis cinerea*. It is to be applied at a rate of 50–75 g/100 L as a foliar spray in grapevines with applications made every 3–14 days, but particularly at flowering, pre-bunch closure, veraison, and pre-harvest. The higher rate is to be used in conditions expected to lead to high disease pressure. It is applied at a rate of 500 g/ha in strawberries, with applications every 3–14 days, particularly at or before flowering.

Application of Serifel Biofungicide should be performed to the point of runoff for dilute spraying, and in an appropriate volume of water ensuring coverage of all foliage and fruit for concentrate spraying; concentrate spraying is allowable at up to two times the dilute spraying rate. Serifel Biofungicide is applied at a fixed rate per hectare in strawberries. A maximum of 10 applications of Serifel Biofungicide may be made annually.

8.2 Efficacy and target crop safety

Efficacy

The applicant, BASF Australia Ltd, presented results from fourteen replicated Australian small plot field trials on efficacy in grapevines and strawberries from 2013–2015. Additional data were supplied from one New Zealand trial and three European trials on efficacy in grapevines from 2012–2014. In the trials sprays were applied at key stages and over flowering and prior to infection. Serifel Biofungicide was applied either as a stand-alone product or in conjunction with sprays of standard fungicides. *Botrytis cinerea* infection pressure varied in the trials from low to very high.

Grape vines

Serifel Biofungicide was tested at rates of 10–125 g/100 L water including the proposed label rates of 50–75 g/100 L and up to eight sprays. Eight Australian field trials were conducted in commercial vineyard locations in South Australia, Western Australia, New South Wales and Victoria representative of Australian wine growing regions, as well as trials conducted in New Zealand, Spain and Portugal. Efficacy was assessed on natural and/or induced disease infections in commercial vineyards. Assessments were made on the extent of *Botrytis cinerea* infection in randomly selected grape bunches. Disease incidence was assessed by the presence or absence of *Botrytis cinerea* as a percentage, and the severity by the percentage of bunch area infected. The product was applied as a preventative treatment at key stages in grape development including 10% and 80% cap-fall, and before bunch closure. These treatments were compared to industry standard treatments.

Serifel Biofungicide was trialled as a full-season preventative spray program as either a stand-alone product or in conjunction with sprays of industry standard fungicides. Serifel Biofungicide provided significant control of *Botrytis cinerea* when applied at 50–75 g/100 L in five out of six trials in which significant disease developed, and was as effective as an industry standard fungicide.

Strawberries

Serifel Biofungicide was tested at rates of 100–1000 g/ha including the proposed label rate of 500 g/ha in strawberries, in up to six sprays. Six Australian field trials were conducted in Queensland, South Australia and Victoria, under conditions typical for commercial strawberry production. Efficacy was assessed on natural disease infections. The extent of *Botrytis cinerea* infection was measured as the percentage of fruit with symptoms of disease per plot. Disease incidence was determined as a percentage of strawberries with *Botrytis cinerea* infection, and severity was determined on an objective scale. The product was applied at key stages in strawberry development including prior to or at flowering and through to harvest.

The trials were randomised complete block designs, with four to six replicates and product rates equivalent to that proposed on the label as well as higher and lower rates. Spray volumes used were in the range of normal commercial practices. The trials were designed to test the efficacy of the product as a stand-alone product, and as part of a preventative program.

Adequate controls and comparison with industry standard fungicides in each trial were included in the trials reported. The data were analysed appropriately. In all trials the treatments were replicated, statistical analyses were undertaken, and assessments of crop safety were conducted at several stages throughout each of the trials.

Serifel Biofungicide was trialled as a full-season spray program and was applied at key stages in strawberry development including prior to or at flowering and through to harvest at rates of 100–1000 g/ha. Serifel Biofungicide at the label rate of 500 g/ha was effective in significantly reducing *Botrytis* bunch rot in three out of four strawberry trials in which disease developed to a moderate level. Serifel Biofungicide was as effective as an industry standard chemical fungicide as well as combinations of commercial fungicides.

Crop safety

No phytotoxic symptoms were observed in any of the trials for grapevines or strawberries. The field trials demonstrated that Serifel Biofungicide was safe to use at rates up to 125 g/100 L (1.67x label rate x 8 applications) in grape-vines with no damage observed in flowers, foliage and fruit. Serifel Biofungicide was also safe to use at rates of 1000 g/ha (2 x label rate) x 7 applications in strawberries, with no damage observed in leaves or fruit.

Resistance management

The bacterium *B amyloliquefaciens* is prevalent in soils and has been found in a variety of habitats worldwide. The MBI 600 strain of *B. amyloliquefaciens* is known to be antagonistic toward fungal plant pathogens. This antagonism is achieved in several ways including nutrient competition, site exclusion, colonisation, and attachment of the bacterium to the fungal pathogen.

The Fungicide Resistance Action Committee (FRAC), has designated *B. amyloliquefaciens* strain MBI 600 as a Group 44 fungicide, the mode of action has been defined as being a microbial disrupter of pathogen cell membranes. The risk of the development of resistance is thought to be low as the mode of action of *B. amyloliquefaciens* MBI 600 is achieved by a range of mechanisms and does not rely solely on a single site of action.

8.3 Recommendations

Trial data support that Serifel Biofungicide will provide acceptable control against *Botrytis* bunch rot (*Botrytis cinerea*) on grape vines, and against grey mould (*Botrytis cinerea*) on strawberries when used as directed. Acceptable crop safety is expected when the product is used as directed. The directions for use are appropriate and consistent with fungicide use in commercial agriculture in Australia.

9 LABELLING REQUIREMENTS

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Serifel Biofungicide

ACTIVE CONSTITUENT: 110 g/kg (>5.5 x 10^{10} cfu/g) *Bacillus amyloliquefaciens* strain MBI600

GROUP **44** FUNGICIDE

For the control of *Botrytis cinerea* in grapes and strawberries

IMPORTANT: READ THE ATTACHED LEAFLET BEFORE OPENING OR USING

CONTENTS: 50 g, 500 g, 1 kg, 2 kg, 2.5 kg, 5 kg, 10 kg, 20 kg, 2 x 500 g, 4 x 500 g, 5x 500 g, 10 x 500 g

BASF Australia Ltd ABN 62 008 437 867
Level 12, 28 Freshwater Place Southbank VICTORIA 3006

DIRECTIONS FOR USE

RESTRAINTS
DO NOT apply during rain or if rain is expected.
DO NOT apply by aircraft.
DO NOT apply more than 10 applications per growing season.
DO NOT apply more than 5 kg/ha per growing season.

CROP	DISEASE	RATE	CRITICAL COMMENTS
Grapevines	Botrytis bunch rot / Grey mould (*Botrytis cinerea*)	50–75 g/100 L	Apply Serifel preventatively, prior to an infection period and the development of disease. Continue applications on a 3–14 day interval as required, when conditions favour botrytis infection and development. Use the higher rate when high disease pressure is expected Key application timings include flowering, pre-bunch closure, veraison and pre-harvest. Serifel is best applied as part of an integrated botrytis management program. Mix and apply Serifel in a sufficient volume of water to ensure uniform dispersion in the spray tank and thorough coverage of foliage, flowers and fruit. Apply by dilute or concentrate spraying equipment. Apply the same total amount of product to the target crop whether applying this product by dilute or concentrate spraying methods. For concentrate spraying do not use at rates greater than 2 times the dilute spraying rate (ie at a concentration factor greater than 2X) – refer 'Application' section in GENERAL INSTRUCTIONS
Strawberries	Grey mould (*Botrytis cinerea*)	500 g/ha	Apply Serifel preventatively, prior to an infection period and the development of disease. Continue applications on a 3–14 day interval as required, when conditions favour botrytis infection and development. Key application timing commences at or before flowering. Serifel is best applied as part of an integrated botrytis management program. Mix and apply Serifel in a sufficient volume of water to ensure uniform dispersion in the spray tank and thorough coverage of foliage, flowers and fruit.

NOT TO BE USED FOR ANY PURPOSE, OR IN ANY MANNER, CONTRARY TO THIS LABEL UNLESS AUTHORISED UNDER APPROPRIATE LEGISLATION.

WITHHOLDING PERIODS:
Not required when used as directed

GENERAL INSTRUCTIONS

MIXING

Before use ensure that all application equipment is clean. Add half the required volume of water and start agitation. Add the required quantity of Serifel. Fill the tank to the required volume whilst maintaining agitation. Continuous agitation must be maintained until spraying is complete.
Following storage, Serifel biofungicide may take longer to disperse. To ensure good dispersion, premix with a small amount of water.

All application equipment should be cleaned thoroughly with water prior to storage.

APPLICATION

Dilute Spraying

♦ Use a sprayer designed to apply high spray volumes, up to the point of run-off and matched to the crop being sprayed.
♦ Set up and operate the sprayer to achieve even coverage throughout the crop canopy. Apply sufficient spray solution to cover the crop to the point of run-off. Avoid excessive run-off.
♦ The required spray volume to achieve point of run off may be determined by applying different test volumes, using different settings on the sprayer, or from industry guidelines or other expert advice.
♦ Add the amount of product specified in the Directions for Use Table for each 100 L of water. Spray to the point of run-off.
♦ The required dilute spray volume to achieve point of run off will change and the sprayer set up and operation may also need to be changed, as the crop grows.

Concentrate Spraying

♦ Use a sprayer designed and set up for concentrate spraying (that is a sprayer which applies spray volumes less than those required to reach the point of run-off) and matched to the crop being sprayed.
♦ Set up and operate the sprayer to achieve even coverage throughout the crop canopy using your chosen spray volume.
♦ Determine an appropriate dilute spray volume (See Dilute Spraying above) for the crop canopy. This is needed to calculate the concentrate mixing rate.
♦ The mixing rate for concentrate spraying can then be calculated in the following way:
EXAMPLE ONLY
1. Dilute spray volume as determined above: For example 1000 L/ha
2. Your chosen concentrate spray volume: For example 500 L/ha
3. The concentration factor in this example is: 3 X (i.e. 1000 L ÷ 500 L = 2)
4. If the dilute label rate is 50 g/100 L, then the concentrate rate becomes 2 x 50 (that is 100 g of product per 100 L water for concentrate spraying).
♦ The chosen spray volume, amount of product per 100 L of water, and the sprayer set up and operation may need to be changed as the crop grows.
♦ For further information on concentrate spraying, users are advised to consult relevant industry guidelines, undertake appropriate competency training and follow industry Best Practices.

COMPATIBILITY

For information on the potential to tank mix Serifel with other products, contact your local distributor or BASF.

RE-ENTRY PERIOD

Not required when used as directed

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

DO NOT CONTAMINATE SURFACE WATERS OR DITCHES with chemical or used container

STORAGE AND DISPOSAL

Store in the closed, original container in a dry, cool, well-ventilated area out of direct sunlight.

The product is stable for 34 months if stored between 4°C and 25°C.

50 g–20 kg HDPE CONTAINERS:

Triple-rinse containers before disposal. Add rinsings to spray tank. Do not dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point.

If not recycling, break, crush, or puncture and deliver empty packaging to an approved waste management facility. If an approved waste management facility is not available, bury the empty packaging 500 mm below the surface in a disposal pit specifically marked and set up for this purpose, clear of waterways, desirable vegetation and tree roots, in compliance with relevant local, state or territory government regulations. Do not burn empty containers or product.

Single-rinse or shake remainder into spray tank/water/dip/drench, etc. Do not dispose of undiluted chemicals on site.

1 X 500 g – 10 X 500 g FOIL AND PLASTIC BAGS:

Puncture and deliver empty packaging to an approved waste management facility. If an approved waste management facility is not available, bury the empty packaging 500 mm below the surface in a disposal pit specifically marked and set up for this purpose, clear of waterways, desirable vegetation and tree roots, in compliance with relevant local, state or territory government regulations. Do not burn empty containers or product.

SAFETY DIRECTIONS

Harmful if inhaled. Will irritate the eyes. Repeated exposure may cause allergic disorders. Do not inhale dust or spray mist. Avoid contact with the eyes. When opening the container and preparing the spray wear cotton overalls buttoned to the neck and wrist, a washable hat, disposable dust face mask covering mouth and nose and disposable gloves. If product in eyes, wash it out immediately with water. Wash hands after use. After each day's use wash contaminated clothing

FIRST AID

First aid is not generally required. If in doubt, contact a Poisons Information Centre (Phone Australia 13 11 26) or a doctor.

SAFETY DATA SHEET

Additional information is listed in the Safety Data Sheet.

CONDITIONS OF SALE

All conditions and warranties rights and remedies implied by law or arising in contract or tort whether due to the negligence of BASF Australia Ltd or otherwise are hereby expressly excluded so far as the same may legally be done provided however that any rights of the Buyer pursuant to non- excludable conditions or warranties of the Competition and Consumer Act 2010 or any relevant legislation of any State are expressly preserved but the liability of BASF Australia Ltd or any intermediate Seller pursuant thereto shall be limited if so permitted by the said legislation to the replacement of the goods sold or the supply of equivalent goods and all liability for indirect or consequential loss or damage of whatsoever nature is expressly excluded. This product must be used or applied strictly in accordance with the instructions appearing hereon. This product is solely sold for use in Australia and must not be exported without the prior written consent of BASF Australia Ltd.

APVMA Approval No:

Batch No:

Date of Manufacture:

BASF Australia Ltd

ABN 62 008 437 867

Level 12, 28 Freshwater Place

Southbank VICTORIA 3006

FOR SPECIALIST ADVICE IN AN EMERGENCY ONLY PHONE 1800 803 440 TOLL FREE-ALL HOURS-AUSTRALIA WIDE.

ABBREVIATIONS

ac	Active Constituent
ADI	Acceptable Daily Intake (for humans)
ai	Active Ingredient
APVMA	Australian Pesticides and Veterinary Medicines Authority
ARfD	Acute Reference Dose
bw	Bodyweight
CFU	Colony-forming units
CFU/g	Colony-forming units per gram
d	Day
°C	Degrees Celsius
EC50	Concentration at which 50% of the test population are immobilised
EFSA	European Food Safety Authority
EU	European Union
FRAC	Fungicide Resistance Action Committee
g	Gram
h	Hour
ha	Hectare
HDPE	High-density polyethylene
HPLC	High Pressure Liquid Chromatography or High Performance Liquid Chromatography
id	Intradermal
im	Intramuscular
ip	Intraperitoneal
in vitro	Outside the living body and in an artificial environment
kg	kilogram
L	Litre
LC50	Concentration that kills 50% of the test population of organisms

LD50	Dosage of chemical that kills 50% of the test population of organisms
LR50	Lethal Rate that kills 50% of the test population of organisms
µg	Microgram
mg	Milligram
mL	Millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NCIMB	National Collections of Industrial, Marine and Food Bacteria
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
ng	Nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration Level
NOAEL	No Observed Adverse Effect Level
pH	Potential of hydrogen
PPE	Personal Protective Equipment
RQ	Risk quotient
s	Second
US EPA	United States of America Environmental Protection Agency
WHP	Withholding Period
WP	Wettable Powder

GLOSSARY

Active constituent	The substance that is primarily responsible for the effect produced by a chemical product
Acute	Having rapid onset and of short duration
Carcinogenicity	The ability to cause cancer
Chronic	Of long duration
Codex MRL	Internationally published standard maximum residue limit
Desorption	Removal of a material from or through a surface
Efficacy	Production of the desired effect
Formulation	A combination of both active and inactive constituents to form the end use product
Genotoxicity	The ability to damage genetic material
Hydrophobic	Repels water
Leaching	Removal of a compound by use of a solvent
Metabolism	The chemical processes that maintain living organisms
Photodegradation	Breakdown of chemicals due to the action of light
Photolysis	Breakdown of chemicals due to the action of light
Subcutaneous	Under the skin
Toxicokinetics	The study of the movement of toxins through the body
Toxicology	The study of the nature and effects of poisons

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