Eye PreservedÊ

Assigned INCI Designation: Polyaminopropyl Biguanide

Product Information

Eye PreservedÊ is a broad spectrum, fast acting bactericide. A 20% aqueous solution of poly(hexamethylenebiguanide) hydrochloride, also known as PHMB, **Eye PreservedÊ** is an effective preservative for make-up removers, moisturizing toners, facial cleansers, wet wipes and also offers antibacterial and deodorant properties.

Microbiological Activity Data

The superior antibacterial activity of **Eye PreservedÊ**, reported as MIC (Minimum Inhibitory Concentration (ppm)) for the PHMB active agent, is shown in Table 1.

Table 1. Antibacterial Activity of **Eye PreservedÊ**

Minimum Inhibitory Concentrations (MICs)					
Micro-organism	**Strain No.**	**Eye PreservedÊ (ppm product)**	**Micro-organism**	**Strain No.**	**Eye PreservedÊ (ppm product)**
Bacteria			**Fungi**		
Bacillus subtilis	NCIB 3610	*5*	*Aspergillus niger*	-	*750*
Enterobacter cloacae	NCIB 8271	*40*	*Trichophyton mentagrophytes*	-	*25*
Proteus vulgaris	NCTC 4175	*40*			
Pseudomonas aeruginosa	ATCC 15442	*40*	**Yeasts**		
Pseudomonas putida	-	*25*	*Candida albicans*	ATCC 10231	*300*
Salmonella choleraesius	ATCC 13311	*120*	*Rhodotorula rubra*	NCYC 1659	*7.5*
Salmonella typhimurium	ATCC 14028	*160*	*Saccharomyces cerevisiae*	ATCC 9763	*300*
Staphylococcus aureus	ATCC 6538	*30*			
Enterococcus faecalis	-	*5*			
Streptococcus lactis	NCTC 7944	*20*			

Microbiological Challenge Studies

Studies were run on three formulas using a 1.5% concentration of **Eye PreservedÊ**. The protocol used was a Cosmetic, Toiletry and Fragrance Association (CTFA) Challenge test. All samples were inoculated at the beginning of the study, sampled at 24 hours and weekly for 4 weeks. Samples inoculated with mold spores were generally plated one additional time after 48 hours. Four weeks after the initial challenge, samples were challenged again and the same sampling regime followed.

Key Product Attributes

- a fast-acting broad spectrum anti-microbial
- effective non-formaldehyde, non-paraben preservation
- gentle in-use
- water-soluble
- heat and UV stable

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Eye PreservedÊ Product Data

Make-Up Remover
Base Formulation

Ingredient	%
Deionized Water	q.s. to 100
Propylene Glycol	2.00
Glycerin	2.00
Plantaren	4.00
PEG-8	2.00

Test Results

Test Organism	Unpreserved Control			Test-Eye PreservedÊ		
	Initial Challenge		Re-Challenge	Initial Challenge		Re-Challenge
	24 hrs.	28 days	28 days	24 hrs.	28 days	28 days
S. aureus	*	*	ND	<10	<10	<10
P. aeruginosa	*	*	ND	<10	<10	<10
K. pneumoniae	*	*	ND	<10	<10	<10
C. albicans	*	2.7×10^3	1.8×10^3	<10	<10	<10
A. niger + *Penicillium sp.*	2.7×10^4	1.7×10^2	1.2×10^4	2.0×10^1	<10	<10

** Unpreserved formulation highly contaminated prior to start of test (>10^6) so unable to count the challenge organisms, however, addition of Eye PreservedÊ killed this contamination and the challenge organisms.*
ND = Not determined

Mascara
Base Formulation

Ingredient	%
Water	q.s. to 100
Jaguar C	1.00
Glycerin	2.00
Honeyquat 50	1.00
Musol 20	1.00
Brookosome P	2.00

Test Results

Test Organism	Unpreserved Control			Test-Eye PreservedÊ (1.5%)		
	Initial Challenge		Re-Challenge	Initial Challenge		Re-Challenge
	24 hrs.	28 days	28 days	24 hrs.	28 days	28 days
S. aureus	2.0×10^6	5.4×10^6	7.8×10^5	<10	<10	<10
P. aeruginosa	2.7×10^5	>10^7	>10^8	<10	<10	<10
K. pneumoniae	7.9×10^5	3.7×10^5	3.4×10^6	<10	<10	<10
C. albicans	2.9×10^5	8.5×10^7	8.5×10^7	<10	<10	<10
A. niger + *Penicillium sp.*	2.3×10^4	**	**	<10	<10	<10

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Non-Ionic Emulsion

Base Formulation

Phase (A)	%	Phase (B)	%
DI Water	q.s. to 100	Brookswax D	4.50
Glycerin	5.00	GMS 165	4.00
		Mineral Oil	15.00

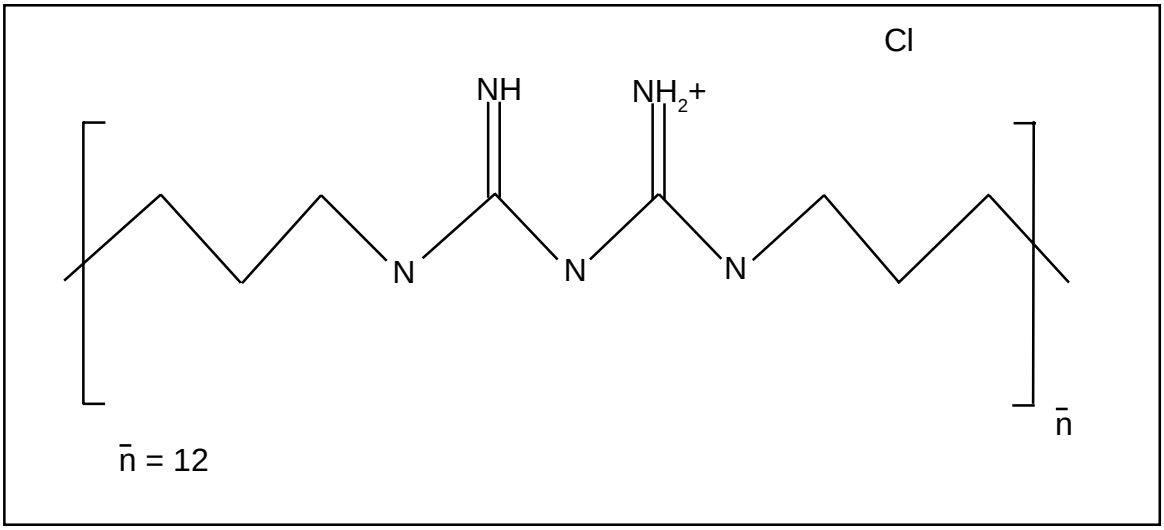
Test Results

Test Organism	Unpreserved Control			Test-Eye PreservedÊ		
	Initial Challenge		Re-Challenge	Initial Challenge		Re-Challenge
	24 hrs.	28 days	28 days	24 hrs.	28 days	28 days
S. aureus	5.9×10^6	***	***	<10	<10	<10
P. aeruginosa	4.2×10^6	3.3×10^6	3.6×10^6	<10	<10	<10
K. pneumoniae	6.3×10^6	6.3×10^5	3.4×10^5	<10	<10	<10
C. albicans	1.2×10^6	1.4×10^6	3.1×10^5	<10	<10	<10
A. niger + *Penicillium sp.*	1.4×10^5	1.7×10^5	1.9×10^5	2.4×10^4	1.2×10^2	1.0×10^1

Eye PreservedÊ Product Data

In the ever-increasing move towards providing a range of effective antimicrobial products, with associated high level of human safety, there has been renewed interest in the development of products based on **Eye PreservedÊ**. Product developers value the features and benefits that **Eye PreservedÊ** affords them, while recognizing the increasing constraints being placed upon them by alternative antimicrobials. **Eye PreservedÊ** is based on the active agent polyaminopropyl biguanide (often referred to as PHMB), as illustrated in Figure 1.

Figure 1. Structure of polyaminopropyl biguanide



Regulatory Information

Polyaminopropyl biguanide is listed in Annex VI of the European Cosmetic Directive 76/768/EEC relating to preservatives for use in cosmetic products, with a maximum authorized use concentration of 1.5% **Eye PreservedÊ**. In the U.S. **Eye PreservedÊ** is listed by the CTFA (Cosmetic, Toiletry and Fragrance Association) in its Cosmetic Ingredient Dictionary. **Eye PreservedÊ** is supported by an extensive toxicology package, which is available upon request. To date **Eye PreservedÊ** is approved for use in the United States, Europe, Japan, Australia, Canada, China, Korea and the Philippines. For products formulated in Japan, **Eye PreservedÊ** should be used at a 0.5% use level (PHMB active level = 0.1%).

Product Information

Eye Preserved™ is effective against a wide range of both Gram-positive and Gram-negative bacteria, such as *Staphylococcus aureus* and *E. coli* 0157, antibiotic resistant bacteria such as MRSA (methicillin resistant *Staphylococcus aureus*) and VRE (vancomycin resistant *Enterococcus*) and odor-causing bacteria.

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Product Data

As a biguanide, **Eye Preserved™** can be classified according to its mode of action as a membrane-active compound. As such, **Eye Preserved™** is either bacteriostatic or bactericidal depending on the concentration, and unlike antiobiotics, there is no risk of organism resistance developing. The anti-microbial effect of **Eye Preserved™** can be described by the following sequence:

- Rapid attraction towards the bacterial surface
- Binding to a receptive site on the surface
- Overcoming bacterial defense/exclusion mechanisms
- Attraction towards the cytoplasmic membrane
- Leakage of low molecular weight cytoplasmic components and inhibition of membrane-bound enzymes
- Extensive disruption of cytoplasmic membrane and leakage of macromolecular components
- Precipitation of cell contents

Recommended additions of **Eye Preserved™** range between 0.2 and 1.5% relative to ready-to-use products, depending on the application and the desired antibacterial effect.

Benefits

- Miscible with water in all proportions
- Remains in the aqueous phase
- Unique biguanide chemistry
  - novel non-specific mode of action
  - no known evidence of development of organism resistance
  - contains no formaldehyde and is not a formaldehyde donor
- Broad spectrum of activity
  - high activity vs. tough Gram (negative) organisms e.g. *Pseudomonas*
- Extensively studied mammalian toxicity
  - low acute toxicity via dermal and oral routes
  - low skin and eye irritancy potential at in-use concentrations
  - low toxicity following long term exposure
  - not teratogenic and shows no reproductive effects when studied over two generations
  - non-genotoxic in a range of studies
  - not considered carcinogenic in humans
- Chemically stable and non-volatile
  - zero VOC
  - easily handled and applied
  - greater than two year storage stability
  - effective and stable over a broad pH range (4-10)
  - active agent heat stable to >140°C
  - UV stable
  - odorless, non-foaming, clear and colorless
- Compatible with a wide range of cosmetic raw materials. As **Eye Preserved™** is cationic, it is compatible with cationic, amphoteric and non-ionic surfactants and is incompatible with strongly anionic systems.

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Product Data

Summary

Eye Preserved™ has been a widely utilized antimicrobial for many years, providing reliable preservation of a diverse range of cosmetic and personal care applications. Although surfactant selection must be considered, various formulation options exist which allow for the development of highly effective consumer products which provide for excellent skin mildness even after repeated application. **Eye Preserved™** offers a gentle and effective option for both preserving and conferring value-added effects to a range of cosmetic and personal care products.

Applications/Use

- Eye make-up removers
- Facial cleansers
- Moisturizing toners
- Skin creams and lotions*
- Hair conditioners
- Impregnated wet wipes

** note compatibility statement above*

Typical Properties

Chemical Composition

Active ingredient:	
Polyaminopropyl biguanide	20%
Inert Ingredients:	
Water	80%
Appearance	Slightly opalescent liquid
Color	Colorless to slightly pale yellow
Solubility	Miscible with water, ethanol, glycerine and propylene glycol
Specific Gravity at 25°C	1.04
pH	5.0 - 5.5
Recommended Use Level	0.2 - 1.5% *depending upon formulation* (ROW excluding Japan) *(0.04 - 0.3% PHMB)* up to 0.5% (in Japan) *(0.1% PHMB)*