OXFORD BIOSCIENCES
Safety Assessment, Analysis, Research & Testing

Oxford Biosciences Ltd.
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COSMETIC PRODUCT SAFETY REPORT

PRODUCT: CBD Muscle Rub Gel

DATE: 30 March 2020

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PART A – Cosmetic Product Safety Information

1. Quantitative and qualitative composition

	Ingredient INCI name	CAS	Function	Limits	Amount
1	Aqua	7732-18-5	Solvent		95.00
2	Glycerin	56-81-5	Denaturant, humectant,		10.00
3	Carbomer	9007-20-9 / 9003	Emulsion stabilising, gel		1.00
4	Cannabidiol	13956-29-1	Antioxidant,	not in list	1.00
5	Polysorbate 20	9005-64-5	Emulsifying, surfactant		1.00
6	Phenoxyethanol	122-99-6	Preservative	V/29	0.90
7	Aloe barbadensis leaf powder	85507-69-3	Skin conditioning		0.50
8	Sodium hydroxide	1310-73-2	Buffering, denaturant	III/15a	0.50
9	Sodium hyaluronate	9067-32-7	Humectant, skin		0.50
10	Cinnamomum camphora bark oil	92201-50-8 /	Masking, skin conditioning,		0.22
11	Mentha arvensis leaf oil	68917-18-0	Masking		0.22
12	Lavandula angustifolia oil	8000-28-0 /	Masking, tonic		0.22
13	Ethylhexylglycerin	70445-33-9	Deodorant, skin		0.10

Allergens present in this product and estimated amounts*:
Limonene: 0.061248%; Linalol: 0.060874%; Geraniol: 0.001364%

* The presence of these allergens must be indicated in the list of ingredients when their concentration exceeds: 0.001% in leave-on products or 0.01% in rinse-off products

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2. Physical & chemical properties and stability

2.1.1 Physical/chemical properties of ingredients (substances or mixtures)

See section 1. Quantitative and qualitative composition – additional specification of ingredients.

Ref. 1. 1 **Aqua**

Aqua (water) is a liquid at standard temperature and pressure with the chemical formula H_2O: one molecule of water has two hydrogen atoms covalently bonded to a single oxygen atom.

Ref. 1. 2 **Glycerin**

Glycerin, or glycerol, is a simple polyol compound, with three hydroxyl groups, which is a colourless, odourless, viscous liquid. Glycerin is naturally occurring in all animals and plant matter in combined form as glycerides in fats and oils, or, in intracellular spaces, as lipids. The glycerol backbone is central to all triglycerides, and its molecular formula is $C_3H_8O_3$. In December 2014 the Cosmetic Ingredient Review (CIR) Expert Panel also noted the high frequency of use that is reported for glycerin and the low instances of reports of toxicity, irritation, and sensitisation and that glycerin is GRAS for food packaging and as a multiple-purpose food substance. When considering the safety of glycerin, the Panel noted that it is naturally occurring in animal and human tissues, including the skin and blood. The data demonstrated low oral and dermal toxicity for multiple animal species and humans, in both acute and long-term studies. The CIR Expert Panel concluded that glycerin is safe in the present practices of use and concentration described in this safety assessment.

Ref. 1. 3 **Carbomer**

Carbomer is a synthetic, high molecular weight, nonlinear polymer of acrylic acid, cross-linked with a polyalkenyl polyether. The Carbomer polymers are used in cosmetics and emulsifying agents at concentrations up to 50%. Acute oral animal studies showed that Carbomers-910, -934, -934P, -940, and -941 have low toxicities when ingested. These polymers are hygroscopic and, when exposed to sunlight, they undergo oxidative degradation. Reported impurities for the Carbomer resins include water, benzene, propionic acid, acetic acid, acrylic acid, heavy metals, iron, arsenic, and lead. In 1982 the Cosmetic Ingredient Review Expert Panel called attention to the presence of benzene as an impurity in Carbomers and recommended that every effort be made to reduce it to the lowest possible value. In 1982 the CIR Expert Panel concluded that on the basis of the available information presented and as qualified in the report, the Carbomers are safe as cosmetic ingredients. In its re-review published in March 2003 the Panel acknowledged the industry practice of removing benzene from Carbomers resulting in levels which should be below those shown to have no risk to human health. In its re-review published in 2003 the Panel concluded that the Carbomers are safe as cosmetic ingredients in the present practices of use and concentration.

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2. Physical & chemical properties and stability

2.1.1 Physical/chemical properties of ingredients (substances or mixtures)

See section 1. Quantitative and qualitative composition – additional specification of ingredients.

Ref. 1. 4 **Cannabidiol**

Cannabidiol (CBD) is a naturally occurring cannabinoid constituent of cannabis. CBD is a 21 carbon terpenophenolic compound which is formed following decarboxylation from a cannabidiolic acid precursor. Unlike Tetrahydrocannabinol (THC), CBD does not have any psychoactive effects due to its very low affinity for the cannabinoid CB_1 and CB_2 receptors. In November 2017 The World Health Organisation (WHO) published their report entitled "Cannabidiol" in which the WHO concluded that "CBD is generally well tolerated with a good safety profile. To date, there is no evidence of recreational use of CBD or any public health related problems associated with the use of pure CBD."

Ref. 1. 5 **Polysorbate 20**

Polysorbate 20 is a polysorbate surfactant. It is a polyoxyethylene derivative of sorbitan monolaurate, distinguished from the other members in the polysorbate range by the length of the polyoxyethylene chain and the fatty acid ester moiety. Molecular formula: $C_{58}H_{114}O_{26}$.

Ref. 1. 6 **Phenoxyethanol**

Phenoxyethanol is an aromatic glycol ether with an alcohol moiety, used in cosmetics as a preservative at concentrations below 1%, with the molecular formula $C_8H_{10}O_2$. Phenoxyethanol is made by reacting phenol with ethylene oxide in the presence of a basic catalyst under pressure and with heating; the resulting product is neutralised, and purified to the point where 4-8% of the Phenoxyethanol is converted to the diethoxylate, thereby reducing the free phenol content. In 1990 the Cosmetic Ingredient Review (CIR) Expert Panel concluded that Phenoxyethanol is safe for use as a cosmetic ingredient in the present practice of use and concentration detailed in this safety assessment. In 2011 The CIR Expert Panel reconfirmed that conclusion.

Ref. 1. 7 **Aloe barbadensis leaf powder**

Aloe barbadensis leaf powder is the powder obtained from the dried gound leaves of the aloe, Aloe barbadensis, Liliaceae

Ref. 1. 8 **Sodium hydroxide**

Sodium hydroxide is a metallic base and alkali salt with the molecular formula NaOH. It is produced by treating oxides with water, known as brine electrolysis. In June 2015 The Cosmetic Ingredient Review Expert Panel noted that in humans, sodium hydroxide was irritating at concentrations as low as 0.5%. The US Food and Drug Administration (FDA) includes Sodium hydroxide on its list of substances affirmed as Generally Recognised as Safe (GRAS) for direct addition to food. Sodium hydroxide is safe in the present practices of use and concentration as described in this safety assessment.

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2. Physical & chemical properties and stability

2.1.1 Physical/chemical properties of ingredients (substances or mixtures)

See section 1. Quantitative and qualitative composition – additional specification of ingredients.

Ref. 1. 9 **Sodium hyaluronate**

Sodium hyaluronate is the sodium salt of hyaluronic acid, a glycosaminoglycan found in various connective, epithelial, and neural tissues. Sodium hyaluronate is a long-chain polymer containing repeating disaccharide units of Na-glucuronate-N-acetylglucosamine.

The safety of Sodium hyaluronate has been assessed by the Cosmetic Ingredient Review (CIR) Expert Panel. The CIR Expert Panel evaluated the scientific data and concluded that Sodium hyaluronate was safe as a cosmetic ingredient.

Ref. 1. 10 **Cinnamomum camphora bark oil**

Cinnamomum camphora bark oil is the volatile oil expressed from the bark of the Camphor, Cinnamomum camphora (L.), Lauraceae

Cinnamomum camphora (commonly known as Camphor tree, Camphorwood or camphor laurel) is a large evergreen tree native to China south of the Yangtze River, Taiwan, Japan, Korea, and Vietnam. Camphor oil's main constituents are 1,8-cineole,α-pinene, camphene, β-pinene, sabinene, phellandrene, limonene, γ-terpinene, and ρ-cymene.

Ref. 1. 11 **Mentha arvensis leaf oil**

Mentha arvensis leaf oil is the oil derived from the leaves of the Horse mint, Mentha arvensis L., Labiatae.

Ref. 1. 12 **Lavandula angustifolia oil**

Lavandula angustifolia oil is the volatile oil obtained by the steam distillation of the flowers of the Lavender, Lavandula angustifolia, Labiatae. The majority of constituents are monoterpenols and esters.

Ref. 1. 13 **Ethylhexylglycerin**

Ethylhexylglycerin is an alkyl glyceryl ether in which the ethylhexyl group is bound to glycerin at one end by an ether linkage as the condensation product of 2-ethylhexanol and glycerin. Its molecular formula is $C_{11}H_{24}O_3$

Ethylhexylglycerin's efficacy as a preservative enhancer is derived by reducing interfacial tension on the cellular walls of micro-organisms, promoting rapid destruction across a wider spectrum. In 2013 the Cosmetic Ingredient Review (CIR) Expert Panel concluded that Ethylhexylglycerin is safe for use as cosmetic ingredient in the present practice of use and concentration detailed in this safety assessment.

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PART A – Cosmetic Product Safety Information *continued*

2. Physical & chemical properties and stability *continued*

2.1.2 Physical/chemical properties of the cosmetic product

Appearance	Cream/Paste/Gel
Colour	White
Aroma	Fragrance free
pH	5.2

*RP: Responsible Person: Taylor Mammon CBD

2.2 Stability of the cosmetic product

The ingredients used in the production of the cosmetic product comply with the relevant legal regulations.

Both the product and constituent ingredients are stable under normal use and warehousing conditions during the entire time of the PAO period.

2.2.1 Taylor Mammon CBD confirms that all product stability tests reflect the stability of the product which is to be placed on the market.

2.2.2 Taylor Mammon CBD uses a PAO based on the results of Taylor Mammon CBD 's stability testing, including shelf life stability testing.

2.2.3 This product was subjected to Preservative Efficacy Testing and proved that it did not support microbial growth. PET reference: Melbec Microbiology 3595.2

3. Microbiological quality

3.1.1 Microbiological specification of ingredients (substances and mixtures).

Based on available information from the ingredient specification (see section 1. Quantitative and qualitative composition– specification of ingredients), the ingredients used can be assessed as microbiologically safe.

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3.1.2 Microbiological specification of the finished product

The given cosmetic product can be regarded as microbiologically safe for consumers' health under the ISO 29621:2010 standard "Cosmetics -- Microbiology -- Guidelines for the risk assessment and identification of microbiologically low-risk products".

The microbiological harmlessness of the ingredients and the cosmetic product is assessed according to COLIPA: Guideline for Microbiological Quality Management (MQM).

This product was subjected to Preservative Efficacy Testing and proved that it did not support microbial growth. PET reference: Melbec Microbiology 3595.2

4. Impurities, trace amounts of forbidden substances, & information about packaging material

4.1 Impurities and trace amounts of forbidden substances

According to specifications (see section 1. Quantitative and qualitative composition – specification of ingredients) submitted by ingredient suppliers, the ingredients do not contain impurities or trace amounts of forbidden substances.

4.2 Information about packaging material

The packaging material applied is suitable for the given type of cosmetic product and meets the predictable use requirements.

Container	Bottle
Container Material	PET
Airless Container	No

The available research suggests that the concentration of phthalates in the contents of PET bottles varies as a function of the contents of the bottle, with phthalates leaching into lower pH products. Temperature also appears to influence the leaching both of phthalates and of antimony from PET, with greater leaching at higher temperatures.

The evidence also suggests that PET bottles may yield endocrine disruptors under conditions of common use, particularly with prolonged storage and elevated temperature.

Therefore it is advisable, in using PET containers, to ensure a minimum pH of 4.0 and to store products at cooler temperatures using a shorter BBE period.

Taylor Mammon CBD confirms that the results of reference sample monitoring show no reaction between the packaging material and the product during the product's stated minimum useable life. During that life no changes to physical and chemical properties of the product were noticed that would affect its usability and safety.

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5. Normal and reasonably foreseeable use

The current label advice:

For external use only, avoid direct contact with the eyes. Keep out of reach of children. Store in a cool dry place out of direct sunlight.

The label of this cosmetic product should include this special note regarding its use, in compliance with Article 19(1)(d) of *Cosmetic Regulation* (EC) No. 1223/2009:

No additional wording is recommended.

6. Exposure to the cosmetic product

Area of application	Body
Product type: Leave-on or Rinse-off	Leave On
Duration and frequency	2.28
Possible additional routes of exposure	Face
Estimated skin surface area (cm^2)	15670
Estimated amount of the product applied according to the SCCS (g/day)	7.82 g
Estimated retention factor according to the SCCS	1
Target group	Adult
Calculated relative daily exposure according to the SCCS (mg/kg bw/day)	123.2

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7. Exposure to the ingredients

	Ingredient INCI name	Concentration	SED
1	Aqua	0.95000	117.04000
2	Glycerin	0.10000	12.32000
3	Phenoxyethanol	0.00900	1.10880
4	Ethylhexylglycerin	0.00100	0.12320
5	Carbomer	0.01000	1.23200
6	Aloe barbadensis leaf powder	0.00500	0.61600
7	Sodium hydroxide	0.00500	0.61600
8	Sodium hyaluronate	0.00500	0.61600
9	Cinnamomum camphora bark oil	0.00220	0.27104
10	Mentha arvensis leaf oil	0.00220	0.27104
11	Lavandula angustifolia oil	0.00220	0.27104
12	Cannabidiol	0.01000	1.23200
13	Polysorbate 20	0.01000	1.23200

***SED**: Systemic Exposure Dose*

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8. Toxicological profile of the ingredients in the formulation

	Ingredient INCI name	MOS
1	Aqua	854.40870
2	Glycerin	1022.72730
3	Phenoxyethanol	1136.36360
4	Ethylhexylglycerin	16233.76620
5	Carbomer	1623.37660
6	Aloe barbadensis leaf powder	8116.88310
7	Sodium hydroxide	162.33770
8	Sodium hyaluronate	1298.70130
9	Cinnamomum camphora bark oil	12064.63990
10	Mentha arvensis leaf oil	4427.39080
11	Lavandula angustifolia oil	15680.34240
12	Cannabidiol	6493.50650
13	Polysorbate 20	4058.44160

***MOS**: Margin of Safety*

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8. Toxicological profile of the ingredients in the formulation - continued

Based on the calculation of MoS (Margin of Safety) for ingredients that can be classified as hazardous to human health, the product does not contain ingredients with toxicologically significant profiles in terms of consumer health.

An ingredient with an MoS above 1000 is considered safe. An ingredient with an MoS above 100 but lower than 1000 must be further considered by the assessor.

In line with WHO guidelines, recommending a minimum value of 100, it is generally accepted that the MoS should at least be 100 to conclude that a substance is safe for use. Since the ingredients used in this formulation have a long worldwide history of use and have an MOS value above 100 then the conclusion is that they are safe for use in this formulation.

9. Undesirable effects and serious undesirable effects

The cosmetic product with a similar composition has been supplied to the market in the long term and until nowadays, no undesired effects to human health have been noticed in relation to the use of this product. Therefore, no undesired effects are anticipated at the common and reasonably predictable application of the given cosmetic product.

After its launch, the cosmetic product will be further monitored by Taylor Mammon CBD in accordance to procedures detailed in *Cosmetic Regulation* (EC) No 1223/2009. The safety of the product should be reviewed on a regular basis. To that end, undesirable and serious undesirable effects on human health during in market use of the product should be filed (complaints during normal and improper use, and the follow-up done) and details forwarded to the safety assessor.

The safety assessor will then update the Cosmetic Product Safety Report (CPSR) based on the new findings and the adopted corrective measures.

10. Additional information on the product

No additional information is available and no additional studies were carried out.

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11. References

- THE SCCS'S NOTES OF GUIDANCE FOR THE TESTING OF COSMETIC SUBSTANCES AND THEIR SAFETY EVALUATION 8TH REVISION
  http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:342:0059:0209:en:PDF
- MSDS of ingredients
- Commission Implementing Decision of 25th November 2013 Guidelines on Annex I to Regulation (EC) No 1223/2009 of the European Parliament and of the Council on cosmetic products
- SCCS - Opinions
  http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm
- CosIng: the European Commission database on cosmetic substances
  http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.simple
- REGULATION 1223/2009 ANNEXES
  http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=ref_data.annexes_v2

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PART B – Cosmetic Product Safety Assessment

1. Assessment conclusion

Based on the information supplied, the cosmetic product detailed in this report is safe for human health when used in common or reasonably predictable conditions in compliance with the instructions provided for the consumer.

This conclusion is only applicable to this cosmetic product with the composition, properties, purpose, and method of use of which are detailed in this documentation, and laboratory tests attached to this assessment, including the detailed production and labelling which has been assessed as meeting the requirements of *Cosmetic Regulation* (EC) No. 1223/2009 effective on the date this report was issued.

2. Labelled warnings and instructions of use

The label of this cosmetic product should include this special note regarding its use, in compliance with Article 19(1)(d) of *Cosmetic Regulation* (EC) No. 1223/2009:

No additional wording is recommended.

Allergens present in this product and estimated amounts*:

Limonene: 0.061248%; Linalol: 0.060874%; Geraniol: 0.001364%

* The presence of these allergens must be indicated in the list of ingredients when their concentration exceeds: 0.001% in leave-on products or 0.01% in rinse-off products. Only the allergen, not the estimated amount, is required on the label.

3. Reasoning

Based on the formulation of this cosmetic product, its qualitative and quantitative composition according to its INCI ingredients, basic physical and chemical characteristics and microbiology, Preservation Challenge Test performed, classification of the cosmetic product type, including its purpose and method of application, and available toxicological information and safety sheets of the ingredients used, the cosmetic product safety has been assessed for the consumer by assessing the toxicological profile of all ingredients, their chemical structure, exposure level and Margin of Safety (MoS) depending on the purpose of use in this cosmetic product.

This cosmetic product contains only the allowed ingredients in allowed concentrations. For ingredients with safety limits as specified in Annexes to *Cosmetic Regulation* (EC) No. 1223/2009, no ingredient exceeds the allowable safety limit therefore is a safe concentration in this cosmetic product. The evaluation of the entire composition and applied ingredient concentrations indicate that as a whole the composition of this cosmetic product complies with the requirements of *Cosmetic Regulation* (EC) No. 1223/2009 of the European Parliament and of the Council.

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4. Assessor's credentials and approval of Part B

Safety Assessor: Allison Wild
Oxford Biosciences Ltd.
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Experience and qualifications:

- MSc in Clinical Pharmacology, University of Oxford
- 10+ years experience formulating cosmetic products
- Full member of the Society of Cosmetic Scientists (SCS)
- Member of the British Pharmacological Society

Signature

30 March 2020

Date