PART B – Cosmetic Product Safety Assessment

1. Assessment Conclusion

We confirm that the product is safe in the stated application when used under normal and reasonably foreseeable use, and the product composition complies with EC Regulation 1223/2009 and all its annexes.

Systemic toxicity, including reproductive / developmental toxicity:	No concerns
Carcinogenicity / Mutagenicity	No concerns
Skin sensitisation	No particular concerns based on skin sensitisation data from animal or human studies on individual ingredients and their concentrations in the product, but there is always a chance that an individual may have a rare reaction to a particular ingredient.
Skin irritancy	No concerns
Eye irritancy	No particular concerns but any foreign matter in the eye will have a tendency to irritate.
Phototoxicity and photosensitisation	No concerns
Microbiological safety	No concerns
Impact of product stability on safety	No concerns
Packaging safety issues	No concerns
Formation of toxic materials via chemical reaction	No concerns
Potential physical/flammability hazards	No concerns

2. Safety assessor's warnings and specific instructions required for safe use

The following warnings are required on both the inner and outer packaging

No particular warnings required

It is assumed that instructions or use of commonplace product type names (e.g. "hand wipes") as described in section 6 of Part A are used. No particular extra instructions are required for the safe use of this product.

3. Reasoning

(a) Potential systemic toxic effects

Table 9 gives the margin of safety for each of the ingredients used. It takes into account all systemic toxicity end points including organ toxicity, reproductive and developmental toxicity, blood and metabolic effects, and carcinogenicity. The end point that drives the NOAEL or other repeat dose toxicity value is given in the critical toxicity effect column, and is usually derived from repeat dose animal studies. If none is written it means that no toxicity was seen at the highest dose tested. Dermal absorption is the main route of entry but the possibility of inhalation and ingestion has also been considered. All the ingredients used are considered safe because they have a margin of safety (MOS) of 100 or over or, for ingredients for which safe levels in the human diet have been calculated, have a margin of exposure (MOE) of 1.0 or greater.

The lowest margin of safety in this product is for phenoxyethanol with a MOS value of 560.

(b) Carcinogenicity / mutagenicity / reproductive toxicity (CMRs)
None of the ingredients as added have harmonised classifications in the EU as carcinogens, mutagens or reproductive toxins (class IA, 1B or 2 under GHS). For those ingredients that do not have a harmonised classification, none are considered to be mutagenic based on weight of evidence of in vitro studies or/and vivo studies.

(c) Potential skin sensitisation effects
The main causes of skin sensitisation in cosmetics are perfume ingredients, essential oils and perfuming absolutes, certain other non-perfuming plant extracts containing high concentrations of terpenes, some preservatives, some hair dyes, and some UV filters.

(c1) Potential skin sensitisation from perfumes, synthetic aromas, essential oils and absolutes: The International Fragrance Research Association (IFRA) has a series of regulations designed to prevent sensitisation to perfumes, essential oils and absolutes. The maximum concentrations of various ingredients for different types of cosmetic products (in %) are based on a NESIL value (No Expected Sensitisation Induction Level) in $\mu g/cm^2$ from weight of evidence of both human (e.g. RIPT) and animal (e.g. mouse LLNA) studies. The calculations include a safety factor (SAF) of between 30 and 300 including a factor of 10 for inter-individual variability, as summarised in "Dermal Sensitization Quantitative Risk Assessment (QRA) for Fragrance Ingredients, IFRA Technical Dossier 2006". For a few perfuming actives such as Hydroxyisohexyl 3-Cyclohexene Carboxaldehyde (Lyral) this QRA method has not been undertaken due to lack of data, but provisional limits have been derived by IFRA based on other, e.g. epidemiological, evidence. For perfumes, we have checked the relevant IFRA certificate and confirmed that the concentration of perfume complies in this product. For essential oils, absolutes and hydrosols, we have checked the maximum likely level of any IFRA regulated components and sensitisers and we confirm that the product complies with the regulations.

(c2) Potential skin sensitisation from other ingredients: The use of preservatives, UV filters and hair dyes is controlled by the EU on Annexes VI and VII and all toxicity endpoints, including skin sensitisation, are taken into account before an ingredient is listed. This product complies with any maximum concentration restrictions imposed by the Annexes. For most other skin sensitisers (i.e. excluding essential oils and perfumes), the final product would not be considered a risk if the final concentration is less than 0.01%, which is the limit for classification under the CLP regulations. These levels are not exceeded in the product.

(d) Potential skin / eye irritation effects
In the calculation method for classification of mixtures of chemicals under the EU CLP regulations irritation is not significant if the total concentration of individual ingredients classified as category 2 (the lowest hazard category) eye or skin irritants is less than 10% by weight. For leave-on skin-care products we would look for a total of less than 10%, but higher concentrations in rinse-off products can be tolerated on wet skin due to the immediate dilution effect. Dilution with water moderates potential skin irritation but eye irritation can still be serious if product is caught in the eye. The contribution from chemicals classified as corrosive, or as capable of causing serious damage to the eye (H317), has to be taken into account, using higher weighting factors than category 2 irritants. The final pH is also important and the pH should normally be between 3 and 10 to avoid a GHS irritant classification. Some cosmetic ingredients are

classified as irritants (or worse) just because of the pH of the pure ingredient but it would be neutralised in the final product, and this factor also has to be taken into account. The eye irritancy / eye damage classification of some surfactants is due to a combination of the inherent irritancy of the surfactant molecule and the high pH at which it is sold.

Total concentration of ingredients with a classification of irritancy or worse in Table 11 = 0.7%.

Based on the total concentrations of such ingredients and how the product is used, skin and eye irritation are not considered significant.

(e) Potential phototoxicity / photosensitisation
The product does not contain any known phototoxic ingredients.

(f) Microbiological safety
An appropriate preservative challenge test has been carried out and has passed, and every batch is tested for microbial contamination.

It is assumed that the manufacturer is following Good Manufacturing Practice and that microbiological contamination of the final product is being minimised.

(g) Impact of product stability on safety
Given the observations / testing on the product to date, and experience with this type of product, stability is considered satisfactory and is not detrimental in terms of safety. A large increase of pH was seen at 40°C but not room temperature, which should be investigated further and repeated. But if this increase is seen in real time products the pH will not go above 9 and so will not pose a risk of enhanced irritation. The literature indicates that one of the components chlorhexidine gluconate will tend to precipitate at pH's above 8, but this also will not pose a safety risk.

(h) Impact of packaging on safety
No chemical incompatibilities are expected between the primary packaging material (PE sachet contact material and the various wipe substrates)) and the product, and this material(s) is regularly used to package similar cosmetic products in the EU. No deterioration has been seen in the final packaging with previous versions of the product after several years on the market.

It is considered unlikely that toxic substances will migrate from the packaging to the product.

(i) Consideration of possible chemical reactions
Our examination of possible reactive groups and chemical types of ingredients in this product indicates that there are unlikely to be any chemical reactions taking place that will affect the overall safety conclusions. Formation of nitrosamines in this product is not possible.

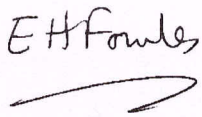
4. Purity conditions
This assessment assumes that only cosmetic, pharmaceutical or food grade ingredients are used. Certain ingredients may have particular purity restrictions imposed on them under the annexes to the EU regulation and this Safety Report is only valid if these requirements are met. Such ingredients are

indicated in Table 12 of Part A. Assuming any restrictions indicated in Table 12 are met, there are unlikely to be significant traces of prohibited substances or Annex III–restricted impurities in the final product, and heavy metals are likely to be below acceptable limits (we use the 2012 Health Canada "technically unavoidable" limits of lead 10ppm, arsenic 3ppm, cadmium 3ppm, mercury 3ppm, and antimony 5ppm as guidance).

5. General notes and conditions of this safety report

a. This safety report has been generated in edit-protected pdf format. It is not valid if any details are manually changed or the report is electronically scanned or altered in any way.
b. This safety report applies to products manufactured, sold or marketed by the company named above. It cannot be transferred or sold to third parties, except with the agreement of EF Chemical Consulting Ltd.
c. This safety report only fully complies with Annex 1 of EC1223/2009 if it is filed in conjunction with the certificates of analysis, IFRA certificates, and safety data sheets for each ingredient. These are provided by the ingredient suppliers. EF Chemical Consulting Ltd does not compile or attach this documentation and the Responsible Person should ensure they are filed together – or provide an electronic link to them.
d. Original versions of challenge test reports, stability testing reports and dermatological testing must also be filed alongside the safety report in the PIF file.
e. The assessment assumes that all other aspects of EC regulation 1223/2009 is being complied with, especially adherence to Good Manufacturing Practices (GMP).
f. Although this document is entitled "Cosmetic Product Safety Report" we do not make any reassurances that the product is considered to be a cosmetic under the EU Cosmetics Regulation. For borderline products we recommend you consult the relevant EU guidance documents and take independent advice.
g. This document does not confirm that we agree with any claims made about the product or implied in the product name. EF Chemical Consulting Ltd is not involved in cosmetic claims support.
h. This assessment applies only to the ingredients listed and the specific application state. A new assessment will be required if a raw material is substituted with a different INCI name, a different colour, or a different perfume or essential oil, or if the same formula is used for a product with a different application.
i. If new undesirable events or "Serious Undesirable Events" are reported then this safety report will require updating.
j. We try to use the European INCI names as listed in the EU's cosing database in the assessments, but we do not guarantee it. Please use our labelling consultancy service if you are unsure of the correct ingredients list to be printed on the label along with the correct perfume sensitisers to be listed.
k. Except for the main preservatives and ingredients where the margin of safety is less than 110, this assessment is valid for concentration variations of +/- 10% of the declared percentage, to allow for manufacturing variations. For products containing water, this assessment is also valid for dilutions of the above formula with up to 5% water, as long as the preservative level is maintained at the same concentration in the finished product.
l. In supplying this safety assessment EF Chemical Consulting Ltd makes no assurances that the individual substances or ingredients are registered or exempt under REACH. This is not usually an issue if the ingredient is sourced within the EU, but importers into the EU are warned that REACH notification rules apply once the annual imported quantity of a particular substance aggregated over all their products exceeds 1 TPA. Even if the substance has been registered it is possible that the registration doesn't cover its use a cosmetic ingredient. Importers into the EU of products containing botanical ingredients derived from endangered species should also make themselves aware of any CITES restrictions. We do not make these checks.

6. Name and signature of assessor



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