BioEstolides – Skin Sensitivity Testing via Cadre-SS

Biosynthetic® Technologies
Biosynthetic® Technologies is a specialty product company that supplies BioEstolides™ to the Beauty and Personal Care industry. We produce non-toxic, eco-friendly, sustainable, biobased, biodegradable oils with enhanced performance properties available in commercial volumes. Our vision at Biosynthetic Technology is to deliver high performing, sustainable solutions for a sustainable future.

BioEstolides do not cause skin irritation or allergic reactions.

Products Discussed:

- BioEstolide 30 (BE30)
- BioEstolide 250 (BE250)
- BioEstolide 250-100 (BE 250-100)
- BioEstolide 1300 (BE1300)
- BioEstolide 1300-100 (BE 1300-100)

Cadre Method for Determining Skin Sensitization

According to Annex VII, skin sensitization is one of the mandatory test requirements for product registration under ECHA for sales and distribution in Europe and the UK. The OECD 422E test was developed to determine the molecular interaction with skin proteins. This test has three guidelines: direct peptide reactivity assay, amino acid derivative reactivity assay, and kinetic direct peptide reactivity assay. The first two assays identify hazards and the third identifies strong sensitizers. There are limitations on this test method that can be remedied using computer modeling which are accepted by ECHA.

State-of-the-art computational chemistry techniques can now be incorporated in predictive models, supported by advances in mechanistic toxicology and the exponential growth of computing resources witnessed over the past decade. The CADRE (Computer-Aided Discovery and REdesign) platform relies on quantum-mechanical modeling of molecular interactions that represent key biochemical triggers in toxicity pathways. CADRE-SS is a hybrid model that evaluates skin permeability using Monte Carlo simulations, assigns reactive centers in a molecule and possible biotransformations via expert rules, and determines reactivity with skin proteins via quantum-mechanical modeling.[1]

Biosynthetic Technologies has subjected BioEstolides to the Cadre-SS hybrid model for skin sensitization and allergic reactions. According to the report, BioEstolides were found to be non-sensitizers and do not cause allergic contact dermatitis.

This test was run in lieu of the standard OECD 422E test that has been used in the past as the BioEstolides were not compatible with the test methodology. The results of CADRE-SS were accepted by ECHA as part of our registration in Europe and the UK.

Protanation Score [a]	0
Pred. K_p[b]	-6.2 (M)
Haptenation Mechanism[c]	None
Metabolism[d]	None
Dichotomous Prediction[e]	NON-SENS
Potency Prediction[f]	NON-SENS
Confidence Score[g]	2+3

[a] **Protonation state** is used to distinguish multiple species of the same chemical. Possible entries use the charge of the species, and may take values of 0 or of positively/negatively charged integers.
[b] **Pred. K_p** refers to predicted rate of skin permeation (logarithmic scale in cm/h). Categorization of permeability (H=High, M=Moderate, L=Low) is provided in ellipses. If no haptenation mechanism (viz. below) is identified, the entry is N/A.
[c] **Haptenation mechanism** refers to mechanism of possible covalent binding to skin proteins and peptides. Typical entries include MICHAEL AD (Michael addition), NUCLEO S (nucleophilic substitution), SNAR (nucleophilic aromatic substitution), SCHIFF B (Schiff base formation), ACYL TR (acyl transfer). Two special cases are HZN (hydrazine) and HOAM (hydroxylamine) compounds. If no mechanism is identified, the entry is NONE. Positive mechanistic entry only identifies region(s) of the molecule (highlighted in red in the diagram) where haptenation is possible. The propensity of the molecule to undergo haptenation, and whether this reaction is sufficient to result in a positive prediction for skin sensitization potential, is determined by subsequent quantum-mechanical modeling. If more than one mechanism is identified, the highest potency is used for overall assessment.
[d] **Metabolism** identifies chemicals requiring metabolic activation to react with skin proteins and peptides. Possible entries are YES, NONE or N/A if no haptenation mechanism is identified by the model.
[e] **Dichotomous prediction** refers to binary classification of chemicals as sensitizers or non-sensitizers.
[f] **Potency prediction** refers to categorical classification of chemicals as either extreme, strong, moderate or weak sensitizers. This distinction is based on LLNA EC3% values: extreme (<0.1), strong (≥0.1 – <1), moderate (≥1 – <10), weak (≥10 – ≤100) , non-sensitizer (>100).
[g] **Confidence score** is reported as a sum of a computational accuracy score (0-2) and a metric that reflects parametrical similarity to training set compounds (1-3). Higher score reflects greater confidence in the prediction.

BioEstolide™ Applications

BioEstolides™ are suitable for use in skin care, hair care, sun care and color cosmetics. Using castor based fatty acids as the base of our product lines, we have developed a class of molecules that offer exceptional moisturization, are easy to apply, and have ample playtime. BioEstolides™ offer enhanced oxidative, hydrolytic, and thermal stability. The BioEstolide line is available in multiple viscosity grades to offer the formulator the latitude to create products. Lower viscosity grades offer excellent solubility while the higher viscosity grades disperse heavier particles and can be used as thickener.

BioEstolides™ are used to formulate creams, lotions, balms, gels, serums, aerosols, solids, and solid and gel sticks. In color cosmetics, they are used in tinted moisturizers, foundations, blush, bronzer, highlighters, lip balms, oils and sticks, mascara, and eye make-up. In sun care formulations, they solubilize chemical sunscreens or aid in the dispersion of physical sunscreens for reef-safe products. In haircare, they are used to improve manageability, create shine, and protect the hair cuticle in shampoos, rinse-out conditioners, leave-in conditioners, thermal protectants, hair dyes, hair lighteners, hair relaxers and other styling aids.

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[1] Kostal J, Voutchkova-Kostal A. CADRE-SS, an in Silico Tool for Predicting Skin Sensitization Potential Based on Modeling of Molecular Interactions. Chem Res Toxicol. 2016 Jan 19;29(1):58-64. doi: 10.1021/acs.chemrestox.5b00392. Epub 2015 Dec 21. PMID: 26650775.