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## **“A comprehensive methodology for ensuring safety, quality, efficacy, and regulatory compliance of hyper-personalized cosmetics”**

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### **1. Introduction**

Over the past decade, the demand for personalized cosmetics has more than doubled<sup>1</sup>, driving the industry to develop tailored solutions that meet diverse consumer needs, while maintaining the highest standards for quality, safety, efficacy, and regulatory compliance.

The convergence of artificial intelligence (AI) and formulation expertise now enables the development of highly customized products and routines, built from thousands of possible ingredient combinations with adjustable concentrations<sup>2</sup>. While the EU Cosmetic Regulation (EC No. 1223/2009) stands as one of the most rigorous and stringent regulatory frameworks globally, it does not provide specific guidance for personalized products, highlighting the need for a dedicated compliance strategy.

Ensuring regulatory conformity across all potential product variations requires a robust methodology that addresses validations of quality, safety, stability and efficacy and complete Product Information File. This work presents a comprehensive and scalable approach developed by a multidisciplinary team of toxicologists, regulatory experts, and formulators, illustrated through the case of a personalized conditioner.

### **2. Materials and Methods**

A robust, risk-based methodology was developed to ensure the regulatory compliance of personalized cosmetic products across all potential formulation combinations.

#### **2.1. Definition of a “Formulation Architecture”**

A “Formulation Architecture” for each product category (shampoo, conditioner, moisturizer, serum...), was established by identifying all eligible ingredients within defined concentration ranges (figure 1). Each ingredient of the formulation architecture was considered at its

highest permissible concentration, representing the most stringent conditions for global regulatory evaluation.

This structured approach enabled the creation of a maximizing qualitative-quantitative composition that included:

- A focused selection of textures formulations with core functional ingredients
- An extensive library of active ingredients providing personalized benefits based on individual consumer needs and blended with texture formulation.

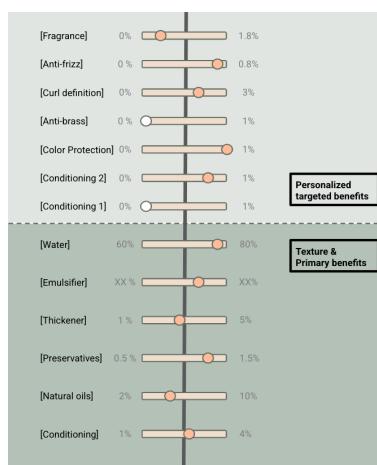


Figure 1. Example of a Formulation Architecture for a conditioner

## 2.2. Collection of a rigorous technical documentation

The technical documentation was collected for all raw materials and packaging components. This included composition data, physicochemical properties, toxicological profiles, and impurity/allergen content.

## 2.3. Testing plan to validate safety, stability and efficacy across formulation combinations

For each product category, a set of scientifically defined formulations was tested:

- Textures formulations only – to establish a general formulation behavior baseline
- Critical formulations – representing the most challenging combinations identified through expert-driven risk profiling
- Realistic formulations – representative of the most common customization patterns that reflect major consumer needs.

These formulations underwent a robust testing matrix aligned with the highest industry standards.

- **Microbiological Safety**

All scientifically defined formulations underwent antimicrobial efficacy testing (Challenge Test) in accordance with ISO 11930:2019.

Formulations were classified as critical based on the risk profile of their ingredients, specifically their potential to support microbial growth or diminish preservative effectiveness (table 1).

Table1. Example of ingredient risk profiling & critical formulation for microbiological quality – Conditioner:

Ingredient category	Risk impact	Example of tested formulations
Water-based actives	May promote microbial growth	<ul style="list-style-type: none"> <li>Texture formulations: each textures combinations + Q.S water</li> </ul>
protein-rich actives	Nutrient source for microorganisms	<ul style="list-style-type: none"> <li>Critical formulation: each textures combination + all actives with high microbial growth potential at maximum concentration</li> </ul>
sugar-rich actives	Nutrient source for microorganisms	<ul style="list-style-type: none"> <li>Critical formulation: each texture combinations + all actives with high microbial growth potential at average concentration</li> </ul>
Glycol-preserved actives	Limited preservation efficacy	
Preservative-free actives	Lacks microbial protection	
Fragrance	Very low water activity	
Oil-based actives	Very low to no water activity	

- **Stability tests**

Stability tests were conducted under accelerated (40°C for 3 months) and real-time conditions (12 months at Room Temperature, 4°C and -18°C).

Critical formulations were specifically designed to test the limits of physical and chemical stability, focusing on key parameters such as viscosity, aspect, color, odor, and pH (table 2)

Table 2. Example of ingredient risk profiling & critical formulation for stability testing – Conditioner:

Ingredient category	Risk impact	Example of tested formulations
Hydrophilic actives	Dilution effect, emulsifying system disruption	<ul style="list-style-type: none"> <li>Critical formulation: Each textures combinations + hydrophilic actives</li> </ul>
Lipophilic actives	Phase separation	<ul style="list-style-type: none"> <li>Critical formulation: Each textures combinations + lipophilic actives</li> </ul>
Cationic actives	Charge-driven interaction	<ul style="list-style-type: none"> <li>Critical formulation: Each textures combinations + hydrophilic actives + cationic actives + Silicone + Fragrance</li> </ul>
Silicones	Affects viscosity and emulsion structure	<ul style="list-style-type: none"> <li>Critical formulation: Each texture combinations + all actives at maximum concentration + Fragrance</li> </ul>
Fragrance	Alters pH, color, odor	<ul style="list-style-type: none"> <li>Realistic formulations: Each texture combinations + actives at average concentration + fragrance</li> </ul>

- Packaging compatibility tests:**

Tests were performed to assess interactions between formulation ingredients and packaging materials using both final packaging and glass control under accelerated and real-time storage conditions. Analytical monitoring included the assessment of impurities, contaminants and key attributes such as pH, appearance, color, odor as well as packaging integrity and functionality.

Critical formulations were specifically designed to challenge potential interactions between formulation ingredients and packaging materials (table 3).

Table 3. Examples of ingredient risk profiling & critical formulation for compatibility testing – Conditioner:

Ingredient category	Risk impact	Example of tested formulations
Lipophilic actives	Component migration, packaging degradation	<ul style="list-style-type: none"> <li>Critical formulation: Each textures combinations + all lipophilic actives + fragrance</li> </ul>
Fragrances	Chemical interactions with packaging	<ul style="list-style-type: none"> <li>Critical formulation: Each textures combination + all pH-altering actives + fragrance</li> </ul>
Extreme pH actives	Structural damage to packaging materials	<ul style="list-style-type: none"> <li>Critical formulation: Each textures combination + all viscosity-altering actives + fragrance</li> </ul>
High viscosity actives	Affects dispensing and packaging functionality	<ul style="list-style-type: none"> <li>Realistic formulation: texture combinations + actives at average concentration</li> </ul>

- Ocular and dermatological tolerance**

Selected formulations underwent:

- In vitro ocular tolerance testing using reconstructed human epithelial tissue models
- Dermatological safety evaluation via 48-hour patch tests and use tests on human volunteers under dermatological supervision.

Critical formulations with the highest theoretical risk of skin or ocular irritation were identified through a systematic ingredient-level risk assessment. This included combinations of ingredients known to impact barrier function, trigger immune responses, or act as common sensitizers (table 4).

Table 4. Examples of Ingredient Risk Profiling & Critical Formulation for safety testing – Conditioner:

Ingredient category	Risk impact	Example of tested formulations
Fragrance, Essential oils	Skin/ocular irritants, high allergenic potential	<ul style="list-style-type: none"> <li>Texture formulations: Each textures combinations</li> </ul>
Tensioactives	May disrupt skin barrier function	<ul style="list-style-type: none"> <li>Critical formulation: Each textures combination + all potentially irritating actives at maximum concentration + Fragrance</li> </ul>
Glycols	May disrupt skin barrier function and increase skin permeability	<ul style="list-style-type: none"> <li>Realistic formulation: Each textures combination + all potentially irritating actives at average concentration + fragrance</li> </ul>
Cationic actives	Charge-related irritation (especially ocular)	
Anionic actives	May cause dermal irritation	
Acid/Bases	pH imbalance; potential corrosivity	
protein-rich actives	May penetrate skin and activate immune response	
Preservatives	Biocidal activity known to trigger irritation or sensitization	
Dyes	Known irritants	
Occlusive film former	May enhance ingredient penetration and irritant potential	
Soothing actives	Supportive against irritation	

- Efficacy Evaluation**

Depending on product type, efficacy was assessed through in vitro testing, use tests, and clinical studies. Baseline formulas containing the minimum effective concentration of active ingredients were tested for core performance, while additional formulations were assessed to support specific product claims.

Illustration – Anti-Breakage Testing for Conditioner:

A key performance indicator was the reduction of hair breakage, assessed using a custom automated grooming simulator. Hair tresses ( $n = 10$  per group) were pre-washed with sulfated shampoo then treated with various texture combinations containing minimal conditioning actives versus untreated. Each hair tress underwent 2,000 combing cycles and broken fibers were collected and counted every 200 strokes.

The average number of broken fibers per group was analyzed using Student's t-test at a 95% confidence level to determine the statistical significance of treatment effects.

### 3. Results

The formulation architecture defined for each product category enabled the creation of a theoretical critical "maximized" formulation, where all potential ingredients were included at their highest allowable concentrations. This critical formulation serves as a representative case to span the full range of possible personalized combinations.

For the conditioner, this approach involved setting each ingredient at the upper limit of its specified range to simulate the most demanding regulatory scenario "the critical maximized formulation"

The integration of detailed data on all raw materials and packaging components allowed for the identification of potential allergens and impurities. This comprehensive dataset supported a rigorous exposure risk assessment and the accurate calculation of safety margins.

In the case of the conditioner, full toxicological documentation including data on impurities, allergens, and cumulative exposure provided the basis for the safety assessor to define ingredient thresholds and assess overall safety, taking into account typical application amounts and usage frequency.

The extensive series of tests carried out on texture formulations, realistic formulations and critical formulations selected via expert-led risk profiling, provided robust evidence to support safety assessors in their evaluation. These results supported the establishment of appropriate warnings, usage instructions, and conditions ensuring safe use under normal and reasonably foreseeable conditions.

Microbiological quality testing confirmed that all critical formulations complied with ISO 11930:2019 – Criterion A, demonstrating effective antimicrobial protection across the entire formulation range.

Stability and compatibility studies showed that all tested formulations remained within specification under both accelerated and real-time storage conditions, allowing for the determination and establishment of a validated shelf life.

Ocular and dermal tolerance evaluations indicated acceptable tolerance profiles for all tested formulations, supporting the inclusion of relevant precautionary statements, such as "in case of contact with eyes, rinse thoroughly with water".

Lastly, efficacy testing demonstrated a significant reduction in hair breakage across all conditioner texture combinations, even those formulated with minimal levels of conditioning active

ingredients. These findings supported the product's performance claims and support compliance with performance labeling requirements.

#### 4. Discussion

This methodology offers a robust and regulatory-aligned framework, fully compliant with EU Regulation (EC No. 1223/2009). It supports the creation of a complete Product Information File (PIF) and provides all necessary elements for the toxicological safety assessment and the preparation of the Cosmetic Product Safety Report (CPSR).

Built on a risk-based approach, the methodology relies on the expertise of formulators to define critical test conditions tailored to each product category and galenic form. This ensures that all formulation combinations can be assessed consistently for safety, quality, and efficacy. Any modification to the initial formulation architecture requires a thorough reassessment of its impact on the risk profile and the validity of prior evaluations.

To ensure global regulatory compliance we provide an integrated methodology that includes:

- Implementation of a manufacturing process compliant with Good Manufacturing Practices (GMP),
- Validation of finished product specifications,
- Preparation of compliant labeling with substantiated claims,
- Strict exclusion of animal testing,
- Establishment of post-marketing surveillance system,
- Notification of products to the competent authorities.

This integrated approach ensures that personalized cosmetic products can be safely brought to market while meeting both regulatory requirements and consumer expectations.

#### 5. Conclusion

This work presents a comprehensive and scalable methodology to ensure the full regulatory compliance of personalized cosmetic products. By integrating a well-defined formulation architecture, expert-led ingredient risk profiling, and rigorous testing across microbiological safety, stability, compatibility, ocular and dermatological tolerance as well as efficacy, the approach allows for the robust evaluation of all possible product combinations.

Applied to a personalized conditioner, this methodology has successfully demonstrated its ability to define critical formulations, validates both safety and performance, and supports the generation of complete regulatory documentation including the Product Information File (PIF) and Cosmetic Product Safety Report (CPSR).

Grounded in EU regulatory requirements and co-developed with toxicology and regulatory experts, this methodology offers a reliable framework for managing the complexity of personalization in cosmetics. It lays the foundation for industry adoption and, upon validation by competent authorities, could serve as a reference model.

Looking ahead, advanced AI-driven automated manufacturing infrastructures will further enable the scalable production of millions of unique formulations, ensuring both personalization and regulatory compliance in a more sustainable way.

### **References:**

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