Barrier Integrity Framework

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Preamble

Most formulations developed for compromised skin barriers are not assessed against the physiological conditions they are intended to address. They are evaluated for safety and stability as required by regulation, but not for physiological coherence: whether their component logic holds under the specific conditions of barrier-impaired skin.

This gap is not a regulatory failure. It is a structural absence. No systematic framework exists for evaluating whether a formulation is coherent for compromised barriers specifically, as distinct from being safe, stable, or effective in general. The Barrier Integrity Framework was developed to provide that assessment.

1. The Assessment Principle

Physiological coherence, as defined by this Framework, is not a claim about efficacy. It is a structural judgment: whether the component logic of a formulation is internally consistent and compatible with the physiological conditions of compromised skin barriers.

A formulation is examined against defined criteria derived from peer-reviewed dermatological and pharmaceutical literature across four dimensions. Each dimension is evaluated independently. The result is a documented analytical position.

> *The Framework does not conduct laboratory testing, clinical trials, or in vitro permeation studies. Assessments are based on mechanistic inference from published evidence, applied consistently across all examined formulations.*

2. The Four Dimensions

The following table provides an overview of the four dimensions, their scope, classification level, and the consequence of non-fulfillment. Detailed criteria for each dimension follow.

Dimension	Scope	Classification	Non-fulfillment
Barrier Architecture	Structural lipid coherence; lamellar organization; TEWL strategy	Level II	Functional incoherence
Functional pH Corridor	pH compatibility with compromised barrier physiology; serine protease regulation	Level III	Safety-relevant — non-compensable
Membrane Compatibility	Absence of membrane-disruptive components; system-level coherence	Level III	Safety-relevant — non-compensable

Dimension	Scope	Classification	Non-fulfillment
Delivery Logic	Active positioning under compromised barrier conditions; vehicle coherence	Level II	Functional incoherence

Level III dimensions are classified as safety-relevant. Non-fulfillment of either Dimension 2 or Dimension 3 is a disqualifying finding, independent of performance in all other dimensions. Level II dimensions address functional coherence and efficacy plausibility.

3. Dimension Criteria

Dimension 1 — Barrier Architecture (Level II)

This dimension evaluates whether the formulation establishes a physiologically coherent barrier architecture. Assessment criteria include:

- Presence of structurally relevant lipids compatible with lamellar organization of the stratum corneum
- A coherent strategy for transepidermal water loss control
- Absence of internal structural contradictions between components

Non-fulfillment indicates that the formulation lacks structural coherence for compromised barrier conditions. This is classified as functional incoherence, not a safety finding.

Dimension 2 — Functional pH Corridor (Level III — Non-Compensable)

This dimension evaluates whether the formulation operates within the functional pH corridor for compromised skin barriers (pH 4.5–5.0) and maintains this range under conditions of use.

pH directly regulates serine protease activity in the stratum corneum. Elevated pH activates kallikrein-related peptidases, accelerates corneodesmosomes degradation, and impairs lamellar body secretion, producing cascading structural failure independent of other formulation properties (Hachem et al., 2003; 2005). A formulation operating outside the functional pH corridor actively destabilizes compromised barriers.

Deviation from the physiological pH corridor is treated as a non-compensable failure condition, irrespective of performance in other dimensions. Non-fulfillment of Dimension 2 is classified as safety-relevant.

Dimension 3 — Membrane Compatibility (Level III — Non-Compensable)

This dimension evaluates whether the formulation is free of components that disrupt the lipid membrane structure of the stratum corneum, and whether the formulation is internally coherent at the system level. Membrane compatibility is evaluated for the formulation as a whole, not ingredient by ingredient.

Components assessed include surfactant systems, penetration enhancers, solubilizers, and emulsifiers with documented membrane-disruptive potential at operative concentrations (Effendy and Maibach,

1995; Williams and Barry, 2004). System-level coherence requires that no component combination produces interactive effects that exceed individual component limits.

Non-fulfillment of Dimension 3 is classified as safety-relevant and is a disqualifying finding independent of all other dimensions.

Dimension 4 — Delivery Logic (Level II)

This dimension evaluates whether active components are positioned to reach their intended site of action under compromised barrier conditions, and whether the vehicle system supports rather than counteracts this positioning.

- Delivery strategy must be coherent with the altered permeability profile of compromised skin
- Vehicle composition must not introduce components that counteract active positioning
- Penetration claims must be mechanistically plausible under the stated barrier conditions

Non-fulfillment of Dimension 4 indicates functional incoherence. It is not classified as a safety finding.

4. Methodological Limits

The Framework evaluates physiological coherence from formulation composition and peer-reviewed literature. It does not conduct laboratory testing, clinical trials, or in vitro permeation studies. Assessments are based on mechanistic inference from published evidence, applied consistently across all examined formulations.

The Framework does not constitute a safety assessment, a regulatory filing, or a medical claim. It does not evaluate general cosmetic efficacy, regulatory compliance, or product safety in the sense defined by applicable cosmetic regulation. These remain the responsibility of the manufacturer.

The Framework addresses a defined and bounded question: whether a formulation is physiologically coherent for compromised skin barriers.

> *Assessments are conducted against the version of the Framework in force at the time of evaluation. Version history is maintained in the Hydra Chronic document registry.*

5. Document Status

Document Status	In Force
Version	1.0
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Ref. Primary Literature

The following sources constitute the core evidence base underlying the Framework criteria. Full methodological documentation for each dimension is maintained in the internal Barrier Integrity Index methodology series.

Bouwstra, J.A. et al. (2003). Structure of the skin barrier. Advanced Drug Delivery Reviews. 55(9), 789–793.

Effendy, I. & Maibach, H.I. (1995). Surfactants and experimental irritant contact dermatitis. Contact Dermatitis. 33(4), 217–225.

Elias, P.E. & Feingold, K.R. (2001). Skin as an organ of protection. Journal of Investigative Dermatology. 116(2), 168–169.

Fluhr, J.W. & Darlenski, R. (2012). Skin surface pH: mechanism, measurement, significance. In: Textbook of Aging Skin. Springer, Berlin.

Hachem, J.P. et al. (2003). pH directly regulates epidermal permeability barrier homeostasis, and stratum corneum integrity/cohesion. Journal of Investigative Dermatology. 121(2), 345–353.

Hachem, J.P. et al. (2005). Sustained serine proteases activity by prolonged increase in pH leads to degradation of lipid processing enzymes and profound alterations of barrier function and stratum corneum integrity. Journal of Investigative Dermatology. 125(3), 510–520.

Hadgraft, J. & Lane, M.E. (2005). Skin permeation: the years of enlightenment. International Journal of Pharmaceutics. 305(1–2), 2–12.

Holleran, W.M. et al. (2006). Sphingolipids are required for mammalian epidermal barrier function. Journal of Lipid Research. 47(9), 2103–2111.

Man, M.Q. et al. (2009). Optimization of physiological lipid mixtures for barrier repair. Journal of Investigative Dermatology. 129(9), 2333–2340.

Noh, S. et al. (2015). Skin pH is the master switch of kallikrein 5-mediated skin barrier destruction in a murine atopic dermatitis model. Journal of Investigative Dermatology. 135(2), 414–422.

Rawlings, A.V. & Matts, P.J. (2005). Stratum corneum moisturization at the molecular level. Journal of Investigative Dermatology. 124(6), 1099–1110.

Schmid-Wendtner, M.H. & Korting, H.C. (2006). The pH of the skin surface and its impact on the barrier function. Skin Pharmacology and Physiology. 19(6), 296–302.

Voegeli, R. et al. (2009). Increased stratum corneum serine protease activity in acute eczematous atopic skin. British Journal of Dermatology. 161(1), 70–77.

Williams, A.C. & Barry, B.W. (2004). Penetration enhancers. Advanced Drug Delivery Reviews. 56(5), 603–618.