

# The Science of Whipped Formulation Technology

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## Formulation Science, Engineering, and Commercial Application of eN<sub>2</sub>fused™ Nitrous Oxide-Infused Bag-on-Valve Formulations

Formulated Solutions · Technical White Paper and R&D Reference

### Executive Summary

Whipped formulation technology turns a conventional lotion, cream, or ointment into a light, structured foam that spreads into a smooth film on contact with skin. Formulated Solutions' eN<sub>2</sub>fused™ platform achieves this by infusing the formulation itself with nitrous oxide (N<sub>2</sub>O) microbubbles and dispensing it from a Bag-on-Valve (BoV) package driven by compressed air.

The architecture has two separate gas roles. Compressed air, held between the bag and the can, is the pressurizing agent that squeezes the bag and drives dispensing. Nitrous oxide is incorporated into the formula as foam-generated microbubbles before it is filled into the bag; when the product leaves the package and returns to atmospheric pressure, that N<sub>2</sub>O expands and generates the whip.

The platform is commercially proven. It underpins marketed products in sun care, eczema and anti-itch care, topical analgesics, and diaper rash care, and it is protected by a portfolio of granted patents in the United States, Europe, and other jurisdictions.

This paper serves two audiences: technical readers at brand owners and development partners evaluating the technology, and Formulated Solutions R&D teams who need a single reference for its science, engineering, and failure modes.

### What this paper covers

- The emulsion science and rheology that make whipped formulations possible
- How N<sub>2</sub>O microbubbles are incorporated, held, and released, and why N<sub>2</sub>O outperforms other gases
- Bag-on-Valve engineering: can, bag, valve, actuator, and compressed-air pressure management

- Formulation design, stability, regulatory, and quality considerations
- Applications, the platform's commercial track record, and its patent estate
- An evaluation framework and a troubleshooting reference for development teams

## How to use this paper

Readers new to the category can read from start to finish. Formulation and packaging scientists will find Sections 2 through 5 most relevant. Regulatory and quality reviewers should start with Sections 6 and 7. Business development and brand teams should start with Sections 8 through 11. Section 12 describes the eN<sub>2</sub>fused™ platform's engineering design, and Section 14 is a troubleshooting reference for development work.

## 1. Introduction

Topical products have long been grouped as creams, lotions, ointments, gels, and foams. These dosage forms remain effective, but consumers now judge products on ease of application, texture, residue, absorption, and overall experience, not efficacy alone.

Whipped formulation technology sits where pharmaceutical science, packaging engineering, and consumer experience meet. In the eN<sub>2</sub>fused™ approach, nitrous oxide is whipped into the formulation as fine microbubbles, and the infused product is sealed inside the flexible bag of a Bag-on-Valve package. Compressed air outside the bag provides the dispensing force. On actuation, the product leaves the package, the N<sub>2</sub>O expands, and the product emerges as a light, whipped ribbon.

A whipped formulation is not simply a lotion with gas added. It is a purpose-built emulsion engineered to hold dissolved and dispersed N<sub>2</sub>O under pressure, resist bubble agglomeration, survive high-shear valve flow, expand on release, and collapse in a controlled way, all while remaining chemically and physically stable across a commercial shelf life.

### 1.1 Why this matters now

Many topical categories have matured around a narrow set of widely available active ingredients that are hard to differentiate on pharmacology alone. Consumers increasingly choose and repurchase products based on how they feel to use. Where the active ingredient can no longer differentiate a brand, the delivery experience often can.

## 1.2 The systems perspective

Whipped formulation performance cannot be understood or engineered by looking at the formulation alone. Formulation, gas incorporation, packaging, manufacturing, and human use are interdependent; a change in one routinely requires a compensating change in another. This systems view, rather than any single ingredient or component, separates a robust commercial platform from a laboratory curiosity.

## 1.3 Scope

This paper covers both the general science of foams and Bag-on-Valve delivery and the specific design of the eN<sub>2</sub>fused™ platform. It is a technical reference; it does not replace product-specific validation data, regulatory submissions, or legal advice.

# 2. Emulsion Science: The Foundation

Every topical emulsion solves the same problem: keeping oil and water, which naturally separate, intimately dispersed for the product’s full shelf life. A whipped formulation adds a third phase, gas, that must also stay finely dispersed under pressure.

## 2.1 Two fundamental architectures

| Type               | Structure                                          | Typical characteristics                                                            |
|--------------------|----------------------------------------------------|------------------------------------------------------------------------------------|
| Oil-in-water (O/W) | Oil droplets dispersed in a continuous water phase | Light feel, fast absorption, minimal residue, easy washability, cooling sensation  |
| Water-in-oil (W/O) | Water droplets dispersed in a continuous oil phase | Rich texture, strong occlusivity, enhanced barrier protection and water resistance |

Neither architecture is inherently superior; the choice depends on the therapeutic objective, desired sensory profile, and positioning. Anhydrous systems such as petrolatum and wax-rich ointments are also strong candidates for N<sub>2</sub>O infusion (Section 3.2).

## 2.2 Why oil and water resist each other

Water is strongly polar and hydrogen-bonds with itself; hydrocarbon oils are largely nonpolar. Mixed without help, the two separate almost immediately, as a shaken vinaigrette does.

## 2.3 Surface tension and the role of surfactants

Creating droplet surface requires energy, and smaller droplets store more of it, so droplets tend to merge. Surfactants, with a hydrophilic head and a lipophilic tail, migrate to the oil–water interface, lower interfacial tension, and form a protective film that slows or prevents coalescence. In whipped systems, the same interfacial chemistry also stabilizes the gas–liquid interface of each microbubble.

## 2.4 Droplet size and distribution

Topical emulsions typically contain droplets from roughly 100 nanometers to 20 micrometers. Distribution matters more than average size: a wide distribution destabilizes faster because larger droplets rise or settle sooner and coalesce more easily. Manufacturing equipment, including rotor-stator mixers, homogenizers, and in-line emulsification systems, largely determines the final distribution.

## 2.5 Mechanisms of emulsion failure

- **Creaming:** droplets migrate upward because of density differences; often reversible.
- **Sedimentation:** dense particles, such as zinc oxide, settle under gravity.
- **Flocculation:** droplets cluster without merging; often a precursor to further instability.
- **Coalescence:** droplets permanently merge, irreversibly reducing interfacial area.
- **Phase separation:** complete failure, compromising dose uniformity and performance.

## 2.6 Building a stable emulsion

Stability comes from several complementary strategies rather than a single ingredient: the surfactant and emulsifier system, polymer networks and thickeners, oil and water phase composition, homogenization energy and temperature, cooling profile, and preservative and packaging compatibility.

### 2.7 The added demands of whipped formulation

A whipped formulation must do everything a conventional emulsion does and also accept saturation with N<sub>2</sub>O, hold a fine microbubble structure under pressure without agglomeration, survive high-shear flow through the valve, expand on release, and collapse in a controlled way on skin. Too little structure and the foam collapses almost instantly; too much and the product is dense and hard to spread. Balancing these forces is the defining challenge of whipped formulation.

## 3. Foam Physics and Nitrous Oxide Incorporation

In the eN<sub>2</sub>fused™ platform, the whip comes from inside the product: N<sub>2</sub>O carried in the formulation expands when the product returns to atmospheric pressure. The package's compressed air only moves the product; it does not create the foam.

### 3.1 Key attributes of a whipped formulation

- Reduced density: feels lightweight rather than heavy or greasy
- High spreadability: covers more area with less rubbing
- Cushioned, plush feel on first contact
- Low-drag application, which may benefit irritated or sensitive skin
- Uniform, metered dispensing
- Premium perception without changing the active ingredient

### 3.2 How nitrous oxide is incorporated and released

The system uses two gases with two distinct jobs.

| Gas                              | Location                               | Role                                                                                                                        |
|----------------------------------|----------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|
| Compressed air                   | Between the bag and the can wall       | Pressurizing agent: squeezes the bag and drives product to the valve                                                        |
| Nitrous oxide (N <sub>2</sub> O) | Within the formulation, inside the bag | Whipping agent: dissolved in and dispersed through the formula as microbubbles, it expands on dispensing to create the whip |

**Incorporation.**  $\text{N}_2\text{O}$  is whipped into the formulation before it is filled into the bag. The gas saturates the formula and is held as a fine microbubble structure throughout the pressurized product. In the finished package, internal pressure of approximately 90–110 PSI keeps the  $\text{N}_2\text{O}$  in solution and compresses each microbubble.

**Containment.** The filled bag is sealed from the compressed-air cavity. The external air pressure squeezes the bag without mixing with the product, which keeps the  $\text{N}_2\text{O}$ -infused formula under pressure and prevents premature foaming.

**Release.** Pressing the actuator meters already-infused product through a controlled orifice. Once outside the package, the compressed microbubbles expand and dissolved  $\text{N}_2\text{O}$  evolves out of the formula, rather like kernels of popcorn popping. The result is a rich, reduced-density whip.

**Modest expansion.** On release, the compressed  $\text{N}_2\text{O}$  microbubbles already held in the product expand roughly 1 to 6 times. Conventional aerosol foams are instead driven by liquefied hydrocarbon propellant droplets, which expand on the order of 120 times as they change from liquid to gas; that tends to produce an airy mousse or a foam that collapses to a thin film. The modest expansion is why the result reads as whipped cream rather than mousse: rich, cushioned, and quick to spread without feeling foamy.

**Why nitrous oxide.**  $\text{N}_2\text{O}$  has a strong affinity for formulation components, particularly lipid- and wax-rich systems, where it performs best. That affinity lets it saturate the formula and form a fine, stable bubble structure. Other gases produce a different result. Nitrogen, for example, still foams, but with its lower affinity for the formulation it creates a different kind of foam and a different application experience.  $\text{N}_2\text{O}$  is what delivers the rich, whipped-cream texture the platform is built around.  $\text{N}_2\text{O}$  also has a long history of use as a whipping gas in food, most familiarly in whipped cream.

### 3.2.1 Handling, safety, and regulatory considerations

Because  $\text{N}_2\text{O}$  is part of the formulation rather than separated from it by the bag, its compatibility with every ingredient, especially the active, must be confirmed during development. Unlike nitrogen,  $\text{N}_2\text{O}$  is not chemically inert. It is a mild oxidizer that can support combustion under some conditions, and it requires appropriate handling, storage, and workplace-safety controls during whipping and filling. Some jurisdictions also regulate its supply because of its anesthetic and psychoactive properties, and it is a greenhouse gas. Requirements vary by market and continue to evolve, so sourcing, worker safety, and consumer labeling are confirmed with EHS and regulatory specialists for each product.

Temperature affects both gases. Gas solubility in liquids generally falls as temperature rises, so warm storage can shift  $N_2O$  from solution into bubbles and promote bubble growth. Compressed-air pressure also rises with temperature. Temperature cycling and transport simulation (Section 6) are therefore essential to confirm foam quality and dispensing across the intended storage range.

### 3.3 Critical formulation variables

- Viscosity modifiers and rheology
- Emulsifier selection
- Droplet size distribution
- Yield stress
- $N_2O$  loading level and bubble architecture
- Lipid and wax content, which strongly influences  $N_2O$  affinity

### 3.4 Bubble architecture and uniformity

The size, distribution, and uniformity of the microbubbles strongly influence sensory feel. Small, uniform bubbles give a smooth, elegant feel and a bright white appearance, since millions of bubbles scatter light back to the eye. Larger bubbles form when microbubbles agglomerate, and they cause both a coarser feel and dispensing defects such as spitting and burping (Section 4.7). Bubble architecture is set jointly by formulation rheology, the whipping process, package pressure, and valve and actuator design.

### 3.5 The engineered transition

The defining feature of a well-designed whipped formulation is the controlled sequence after dispensing:

Stable infused product in the bag → expansion on release → structured ribbon → controlled collapse → elegant film on skin

Too much structure slows spreading; too little reduces visual appeal. Too rapid a collapse eliminates the sensory benefit; too slow a collapse interferes with application. The objective is to optimize the whole sequence, not any single characteristic.

### 3.6 Capillary drainage and foam aging

Foams are metastable. Liquid drains through the channels between bubbles under capillary forces, which ages the foam and eventually collapses it. Understanding drainage kinetics lets formulators set a collapse window that is fast enough to feel responsive and slow enough to preserve the whipped feel while the product is spread.

## 4. Engineering the Bag-on-Valve Platform

Bag-on-Valve is not a conventional aerosol. A traditional aerosol mixes product and liquid propellant in one chamber; a Bag-on-Valve system holds the product in a flexible bag and uses compressed air outside the bag to push it out, so it contains no liquid propellant. The package behaves as a mechanical pressure vessel rather than a chemical propellant system.

### 4.1 Six primary components

| Component                            | Primary function                                                                                                           |
|--------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Container (aluminum can)             | Structural strength, pressure containment, thermal stability, shelf durability                                             |
| Internal bag                         | Holds the N <sub>2</sub> O-infused formulation, sealed from the compressed-air cavity; collapses uniformly for evacuation  |
| Valve assembly                       | Seals the package in storage; meters product during dispensing                                                             |
| Actuator                             | Precision flow-control part that shapes ribbon geometry, exit velocity, and dispensing direction                           |
| Compressed air                       | Pressurizing agent between bag and can; squeezes the bag and drives dispensing                                             |
| N <sub>2</sub> O-infused formulation | The engineered emulsion or ointment carrying dissolved N <sub>2</sub> O and microbubbles that generate the whip on release |

Each component affects performance on its own, but the system performs well only when all six work together. Selecting components one at a time is one of the most common and costly development mistakes.

## 4.2 The container as an active engineering element

The aluminum can provides strength, pressure containment, and shelf durability, and it also shapes pressure behavior. Wall thickness, coating, diameter, height, burst pressure, and buckling resistance influence the volume of the compressed-air cavity and therefore the pressure curve. Aluminum is favored for its strength-to-weight ratio, corrosion resistance, recyclability, dimensional precision, and compatibility with pharmaceutical coatings.

## 4.3 The internal bag

The bag keeps the N<sub>2</sub>O-infused product separate from the compressed air. It must resist chemical attack from the formula, remain flexible, collapse uniformly, limit permeation of both N<sub>2</sub>O and air, survive filling, and keep its seals intact through shelf life. Multilayer laminated films are typically selected for flexibility, chemical resistance, low gas permeability, heat sealability, and durability.

## 4.4 Valve and actuator engineering

The valve seals the package during storage and meters product during dispensing. It contains precision parts, including the stem, spring, housing, gasket, and mounting cup, where small dimensional differences change dispensing behavior. Because the product leaving the valve already contains compressed microbubbles, orifice size controls how the product decompresses as well as how fast it flows.

The actuator is a precision flow-control device, not just a button. Its nozzle diameter, length, expansion chamber, exit geometry, and surface finish set the flow path, exit velocity, ribbon shape, and dispensing direction. Changing only the actuator can transform the consumer experience while the formula stays identical, so actuator selection deserves the same rigor as formulation.

## 4.5 Pressure as a managed design parameter

The compressed air between the bag and the can is the system's only pressure source; there is no liquid propellant reservoir. As product is dispensed, the bag shrinks, the air cavity grows, and pressure falls progressively over the package's life, as expected for a fixed charge of compressed gas.

That pressure decline has two consequences that must be engineered for. First, dispensing force and flow rate must remain acceptable from the first actuation to the last. Second, pressure on the product also keeps N<sub>2</sub>O in solution and microbubbles

compressed, so end-of-life pressure must remain high enough to preserve foam quality and prevent premature foaming inside the bag.

The main design levers are the initial air charge pressure, the ratio of fill volume to can volume, can dimensions, and valve flow characteristics. Charging specifications, in-process pressure checks, and pressure-retention studies are evaluated across the full intended temperature range, because compressed-air pressure rises and falls with temperature.

4.6 Product evacuation

A well-designed system dispenses nearly all of its usable product; the eN<sub>2</sub>fused™ platform achieves greater than 98% evacuation (Section 9.2). Evacuation depends on bag geometry, product viscosity, valve placement, internal friction, and how the bag collapses. It drives consumer satisfaction, value, and sustainability positioning.

4.7 Common failure modes

| Failure mode                      | Typical root causes                                                                                                                               |
|-----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|
| Spitting or burping on dispensing | Microbubbles agglomerating into large gas pockets; insufficient interfacial stability; temperature excursions; poor bubble uniformity at whipping |
| Premature foaming or bag swelling | Product pressure too low to hold N <sub>2</sub> O in solution; air charge loss; late-life pressure decline                                        |
| Weak or inconsistent whip         | Low or variable N <sub>2</sub> O loading; N <sub>2</sub> O loss through bag or seals; formula with low N <sub>2</sub> O affinity                  |
| Valve leakage                     | Damaged gasket, improper crimp, manufacturing defect                                                                                              |
| Poor evacuation                   | Bag folding, high viscosity, valve restriction                                                                                                    |
| Bag rupture                       | Material incompatibility, excessive pressure, filling damage                                                                                      |
| Inconsistent ribbon formation     | Valve variation, actuator mismatch, rheology variation, bubble agglomeration                                                                      |

| Failure mode  | Typical root causes                                           |
|---------------|---------------------------------------------------------------|
| Pressure loss | Compressed-air leakage at seals or crimp, temperature cycling |

4.8 Systems engineering principle

Choosing the valve first, then the actuator, then adjusting the formulation tends to cause unnecessary redesign. A systems approach asks how formulation, N<sub>2</sub>O loading, air pressure, bag, valve, actuator, and manufacturing interact, and lets that guide component selection.

5. Formulation Design Considerations

A whipped formulation must stay physically and chemically stable through manufacturing, whipping, filling, transport, and storage, and then transform in a controlled way on dispensing. That dual requirement separates it from conventional cream or lotion development. Some existing formulas, particularly lipid-rich or structured systems, may be suitable with limited modification, but every formula still requires evaluation and may need reformulation, process, or delivery-system optimization.

5.1 Four interacting structural systems

| System                     | Primary role                                                                                    |
|----------------------------|-------------------------------------------------------------------------------------------------|
| Continuous phase           | Moisturization, solubilization, preservative performance, viscosity, sensory profile            |
| Internal (dispersed) phase | Emolliency, barrier function, skin conditioning, drug solubilization, N <sub>2</sub> O affinity |
| Structural network         | Yield stress, microbubble stabilization, ribbon formation, suspension, dispensing behavior      |
| Interfacial system         | Emulsion stability, bubble formation, resistance to bubble agglomeration, foam persistence      |

## 5.2 Ingredient selection at a glance

- **Oil and wax phase:** influences skin feel, oxidative stability, drug solubility, processing, and N<sub>2</sub>O affinity; lipid- and wax-rich systems generally hold N<sub>2</sub>O best.
- **Water phase:** affects polymer hydration, preservative efficacy, buffer capacity, and manufacturing robustness.
- **Polymers** (natural, synthetic, or associative): build yield stress, suspend internal phases, stabilize microbubbles, and control collapse timing.
- **Emulsifiers:** stabilize oil droplets and gas–liquid interfaces; selected for HLB, electrolyte tolerance, temperature stability, and API compatibility.
- **Humectants** (glycerin, propylene glycol, sorbitol, and similar): influence moisturization, water activity, polymer hydration, and feel.
- **Preservatives:** designed for the product's pH, water activity, and packaging. A one-way Bag-on-Valve dispense reduces contamination during use, but it does not replace a validated preservative system.
- **Oxidation-sensitive ingredients:** because N<sub>2</sub>O is a mild oxidizer in direct contact with the formula, actives and excipients prone to oxidation need compatibility and stability evaluation.

## 5.3 Translating consumer language into engineering targets

| Consumer descriptor | Engineering driver                           |
|---------------------|----------------------------------------------|
| Rich                | Higher yield stress, structured oil phase    |
| Lightweight         | Lower density, controlled expansion          |
| Silky               | Reduced friction coefficient                 |
| Cushioned           | Stable, uniform microbubble architecture     |
| Elegant             | Controlled collapse rate                     |
| Fast absorbing      | Balanced oil composition and rheology        |
| Creamy              | Fine bubble structure and uniform dispersion |

## 5.4 Common development problems and likely causes

- **Foam collapses immediately:** insufficient yield stress, weak polymer network, weak interfacial film, or low N<sub>2</sub>O loading.

- **Foam remains overly rigid:** excessive structure, overbuilt polymer system, or high elastic modulus.
- **Spitting or burping:** microbubble agglomeration in the bag, often from weak interfacial stabilization or non-uniform whipping.
- **Poor ribbon formation:** wrong actuator geometry, unsuitable valve, low viscosity, or excessive flow rate.
- **Poor spreadability:** high yield stress, excessive polymer, or high wax content.
- **Tackiness:** humectant imbalance, polymer choice, slow water evaporation, or high surface friction.
- **Phase separation in storage:** weak emulsifier system, inadequate homogenization, density mismatch, or temperature cycling.

A useful discipline is to ask whether a problem can be solved by changing system architecture, such as the whipping process, N<sub>2</sub>O loading, air charge pressure, valve, or actuator, before adding another ingredient. Many apparent formulation problems start outside the formula, and systems fixes usually produce simpler, more robust products.

## 6. Stability Science: Beyond Chemistry

For N<sub>2</sub>O-infused whipped formulations, stability means more than chemistry: the product must also keep its microbubble structure, dispense consistently, and whip the same way after months of storage, transport, and use.

### 6.1 Four categories of stability

| Category   | What it protects                                                                                                                  |
|------------|-----------------------------------------------------------------------------------------------------------------------------------|
| Chemical   | Active ingredient integrity against oxidation, hydrolysis, photodegradation, and thermal degradation                              |
| Physical   | Resistance to creaming, sedimentation, coalescence, flocculation, phase separation, crystal growth, and microbubble agglomeration |
| Mechanical | Resistance to transport vibration, shaking, inversion, and repeated dispensing                                                    |

| Category   | What it protects                                                                       |
|------------|----------------------------------------------------------------------------------------|
| Functional | Consistency of dispensing, whip quality, ribbon formation, collapse, and spreadability |

A whipped product can meet every chemical specification while its foam quality, ribbon, or dispensing force has drifted. To the consumer the product has changed, even if a traditional stability program shows nothing. That is why advanced delivery systems need this broader definition.

## 6.2 Accelerated and real-world simulation

- **Temperature cycling:** simulates ocean freight, warehouses, vehicles, and bathrooms; checks for bubble growth and agglomeration as  $N_2O$  solubility shifts with temperature.
- **Transportation simulation:** vibration, shock, compression, and orientation changes.
- **Package compatibility:** ingredient adsorption, plasticizer extraction, film permeability to  $N_2O$  and air, and seal integrity.
- **Pressure and gas retention:** compressed-air pressure, valve sealing, leakage, and retention of  $N_2O$  in the formulation over time.
- **Internal structure:** non-destructive imaging such as CT scanning can show whether microbubbles remain fine and uniform or have agglomerated (Section 9.3).

## 6.3 Designing for robustness, not just passing tests

Consumers store products in hot bathrooms, leave them in cars, drop them, and use them intermittently for months. Products should be optimized for those conditions, not for ideal laboratory conditions, so that they thrive in use rather than merely pass stability testing.

## 6.4 Shelf life as a promise

To a regulator, expiration dating marks the period during which a product meets its specifications. To a consumer, it is a promise that the product will perform tomorrow exactly as it does today. Keeping that promise means preserving every characteristic that builds consumer confidence, including the whip itself.

## 7. Regulatory and Quality Considerations

Regulators increasingly treat the container, valve, actuator, and manufacturing process as part of the dosage form rather than as packaging. For whipped formulations this is literally true: the package and the gas are part of how the product works.

### 7.1 Container closure systems

Regulatory review of a Bag-on-Valve product typically evaluates the assembled system, including the bag, valve, gaskets, actuator, overcap, and crimp interface, rather than each component alone.

### 7.2 Extractables and leachables

Extractables are compounds that packaging materials release under aggressive laboratory conditions; leachables are compounds that actually migrate into the product during normal storage. Extractable studies on elastomeric seals, valve gaskets, laminated bag films, adhesives, and coatings identify compounds to follow during stability testing.

### 7.3 Gas incorporated in the formulation

Because N<sub>2</sub>O is part of the finished formulation, its specification, supplier qualification, compatibility with the active and excipients, and any market-specific labeling or supply requirements must be addressed for each product and jurisdiction.

### 7.4 Human factors and dose consistency

Regulators increasingly ask whether users can actuate the package comfortably and intuitively, including elderly and pediatric users. Manufacturers should characterize mass delivered per actuation and its variability across actuations and over the package's life, since compressed-air pressure declines as the package empties. The goal is predictable delivery, not just delivery.

### 7.5 Global regulatory landscape

| Region        | Key authorities and frameworks                                                          |
|---------------|-----------------------------------------------------------------------------------------|
| United States | FDA: NDA, ANDA, 505(b)(2), OTC monographs, MoCRA (cosmetics), combination product rules |

| Region         | Key authorities and frameworks                                                               |
|----------------|----------------------------------------------------------------------------------------------|
| European Union | EMA and national competent authorities; EU Cosmetics Regulation; EU GMP and QP release       |
| United Kingdom | MHRA (independent submissions since Brexit)                                                  |
| Canada         | Health Canada: prescription, non-prescription, natural health product, and cosmetic pathways |
| Australia      | TGA: prescription, OTC, and medical device frameworks                                        |
| Japan          | PMDA: detailed CMC, packaging compatibility, and stability expectations                      |
| South Korea    | MFDS: GMP compliance and harmonized quality principles                                       |
| Brazil         | ANVISA: local registration, GMP inspection, packaging review                                 |

Many markets also reference ICH guidance (Q1 Stability, Q2 Analytical Validation, Q8 Pharmaceutical Development, Q9 Quality Risk Management, Q10 Pharmaceutical Quality Systems, Q12 Lifecycle Management), providing a common scientific framework.

## 7.6 Quality by Design: a practical summary

Quality by Design (QbD) shifts the question from "did this batch pass?" to "why does this product consistently perform?" Development starts with a Quality Target Product Profile (QTPP), from which Critical Quality Attributes (CQAs), Critical Material Attributes (CMAs), and Critical Process Parameters (CPPs) are identified.

| QbD element                  | Examples for whipped formulations                                                                              |
|------------------------------|----------------------------------------------------------------------------------------------------------------|
| Critical Quality Attributes  | Assay, yield stress, microbubble size and uniformity, ribbon formation, evacuation, dispensing consistency     |
| Critical Material Attributes | Polymer molecular weight, oil and wax composition, emulsifier purity, N <sub>2</sub> O grade, valve dimensions |

| QbD element                 | Examples for whipped formulations                                                                                                   |
|-----------------------------|-------------------------------------------------------------------------------------------------------------------------------------|
| Critical Process Parameters | Mixing energy, N <sub>2</sub> O whipping and loading conditions, fill temperature, compressed-air charge pressure, crimp dimensions |

A simplified risk assessment using Failure Modes and Effects Analysis (FMEA) shows how to prioritize development effort:

| Failure mode                      | Potential effect                     | Relative risk |
|-----------------------------------|--------------------------------------|---------------|
| Microbubble agglomeration         | Spitting, burping, coarse foam       | Elevated      |
| Low yield stress                  | Ribbon collapse                      | Elevated      |
| Incorrect valve                   | Poor dispensing                      | Elevated      |
| Variable N <sub>2</sub> O loading | Inconsistent whip                    | Moderate      |
| Polymer variability               | Inconsistent rheology                | Moderate      |
| Air charge pressure variation     | Variable flow, late-life foam change | Moderate      |

Agencies increasingly value scientific understanding over documentation volume. A submission showing risk-based thinking, QbD, and clear engineering rationale typically outperforms one that relies on testing volume alone. This section is general information, not regulatory or legal advice for any specific product.

## 8. Applications Across Categories

N<sub>2</sub>O-infused whipped technology is a versatile platform, already commercialized across several categories (Section 9). It is not right for every topical product, but where it fits the product's objectives it offers a real opportunity to rethink the topical experience.

### 8.1 Prescription dermatology

Chronic conditions such as atopic dermatitis, psoriasis, seborrheic dermatitis, rosacea, acne, and contact dermatitis need frequent, long-term application. Products perceived as greasy, sticky, or hard to spread often see lower adherence despite strong efficacy, so

sensory characteristics become clinically relevant. Whipped delivery is designed to improve application aesthetics without changing the active ingredient, and its lighter feel may suit hair-bearing areas.

## 8.2 Over-the-counter medicines

In crowded OTC categories built on shared actives such as hydrocortisone, tolnaftate, menthol, zinc oxide, lidocaine, and clotrimazole, delivery experience is one of the few meaningful levers for differentiation, because consumers choose for themselves. The platform is already used commercially for hydrocortisone-based eczema and anti-itch care and for topical analgesics.

## 8.3 Sun care

Consumers cite white residue, heavy feel, difficult spreading, and greasiness as barriers to proper application and reapplication, which undermine photoprotection. Whipped delivery is designed to improve spreadability and acceptance, and a whipped sunscreen built on the platform is already on the market (Section 9.1). SPF performance and any comparative claim must still be demonstrated for each formulation.

## 8.4 Cosmetic and prestige skincare

Premium skincare consumers use words like luxurious, airy, silky, cloud-like, and cushioned. These map directly to measurable properties such as yield stress, bubble architecture, and friction coefficient, which makes whipped delivery a natural fit for prestige positioning.

## 8.5 Pediatric and geriatric populations

Caregivers of young children value fast, low-mess application and one-handed use; the visual appeal of a whipped product can also improve a child's acceptance. Older adults benefit from predictable dispensing, low-drag application on fragile skin, and easy spreading despite reduced hand strength or dexterity. Both populations warrant dedicated human factors evaluation.

## 8.6 Wound care, veterinary, and emerging areas

Low-drag application may help where mechanical irritation matters, as in some wound care. Rapid large-area coverage can improve owner compliance and animal comfort in veterinary use. Personalized topical therapy is a longer-term, still-developing direction.

### 8.7 Selecting the right opportunity

Strong candidates for whipped conversion typically share several traits:

- Frequent, daily or near-daily use
- Large treatment areas
- A known adherence problem tied to sensory complaints
- A category that rewards sensory experience
- A real opportunity to differentiate from competitors
- Documented limitations of the current dosage form, such as greasy, heavy, or messy application
- A lipid- or wax-rich base, which generally holds N<sub>2</sub>O best

Products needing ultra-precise dosing, or formulations fundamentally incompatible with N<sub>2</sub>O or gas expansion, may be better served by other technologies. Innovation succeeds when the technology matches the need, not the reverse.

## 9. Platform Track Record

The eN<sub>2</sub>fused™ platform is not a laboratory concept: it has been scaled to commercial production for several brands, characterized with internal imaging, and recognized with multiple industry innovation awards.

### 9.1 Commercial products built on the platform

| Product                                                            | Category             |
|--------------------------------------------------------------------|----------------------|
| Coppertone Whip                                                    | Sun care             |
| Sarna Eczema Relief Whipped Foam (maximum-strength hydrocortisone) | Eczema and anti-itch |
| Blue-Emu                                                           | Topical analgesic    |

Additional prototypes are in development across a broad range of brands and categories. Product names are trademarks of their respective owners.

## 9.2 Demonstration: whipped petrolatum

Petrolatum is an extreme test of the platform: if it can be whipped, almost any lipid-rich base can. In a jar, high-purity petrolatum looks dull and murky, every finger-dip risks contamination, product is hard to retrieve from the bottom, and it applies as a thick glob that must be worked into the skin.

Whipped in the eN<sub>2</sub>fused™ system, the same petrolatum:

- Dispenses bright white, because millions of microbubbles scatter light back to the eye
- Dispenses one way, reducing the in-use contamination risk of repeated finger-dipping
- Achieved greater than 98% evacuation from the Bag-on-Valve package
- Spreads thin in layers, as the outer rim of each bubble melts on contact, rather than sitting as a thick, unctuous glob

## 9.3 Internal structure imaging

Computed tomography (CT) scans of filled whipped Bag-on-Valve packages, taken layer by layer from the bottom of the can to the top, show the microbubble structure inside the product. The scans distinguish the target structure, a fine and uniform microbubble "sponge" throughout the formula, from large agglomerated bubbles. Those agglomerations correlate directly with spitting and burping on dispensing, which makes CT imaging a useful tool for development and troubleshooting.

## 9.4 Design for the user: pediatric diaper rash prototype

An early diaper rash concept shows the platform's experience-first approach. It was designed for one-handed dispensing and application on a moving infant, with a short, wide can for a stable footprint and a twist-to-lock actuator.

## 9.5 Industry recognition

- ADF Personal Care Innovation Award
- SATA Aerosol Innovation Award
- Bayer "Lead for Life" Award, Bayer's highest internal award for technical innovation
- Allure Breakthrough Innovation

## 9.6 Lessons across programs

- Projects start from unmet user needs, not from technology or ingredients.

- Delivery technology is selected because it solves a defined problem.
- Cross-functional development across formulation, packaging, regulatory, manufacturing, and marketing produces stronger outcomes than sequential handoffs.
- Objective measurements, including rheology, imaging, and dispensing data, guide decisions; sensory findings become more valuable when correlated with them.

## 10. Commercial Value

Technical superiority alone rarely guarantees commercial success. A whipped formulation creates value when it solves problems for patients, providers, pharmacists, brand owners, regulators, manufacturers, and retailers, each of whom judges innovation differently.

### 10.1 The economics of differentiation

Many topical markets are commoditized around identical actives. When the active cannot differentiate, companies compete on delivery, convenience, brand trust, and aesthetics, making delivery technology part of the product's core value rather than a cosmetic add-on.

### 10.2 Experience as brand equity

Few consumers can describe a moisturizer's rheology; most can describe how it feels. Engineering the application experience is therefore a form of brand building. Premium positioning often depends less on premium ingredients than on premium execution.

### 10.3 Lifecycle management

As products mature and face generic competition, delivery innovation can renew commercial interest without a new active ingredient. Several commercial whipped products extend established brands in exactly this way (Section 9.1). Regulatory pathways vary by jurisdiction and product type and are assessed case by case.

### 10.4 Patient adherence

Products perceived as messy, unpleasant, or slow to apply are often abandoned, and poor adherence is a major hidden cost in medicine. Better application experience can influence adherence and outcomes, but each product must demonstrate this with evidence rather than assume it.

## 10.5 Selecting a development partner

Choosing a development and manufacturing partner for whipped products involves more than capacity. Key criteria include:

- Expertise in complex emulsions, ointments, and advanced rheology
- Engineering capability across Bag-on-Valve systems, valves and actuators, compressed-air charging, and N<sub>2</sub>O incorporation
- Regulatory experience across prescription, OTC, cosmetic, and device classifications
- Proven scale-up from laboratory prototypes to reliable commercial production

## 10.6 Sustainability

Bag-on-Valve contains no liquid propellant, uses recyclable aluminum, and achieves high product evacuation, all of which support sustainability goals. Actual performance depends on specific materials, manufacturing practices, and regional recycling infrastructure, and should be assessed product by product.

# 11. Intellectual Property

The eN<sub>2</sub>fused™ platform is protected by five patent families covering whipped formulations, thermal stability, high-viscosity and solid ingredients, sensory performance, and gel systems, with granted patents in the United States, Europe, and multiple other jurisdictions.

## 11.1 The eN<sub>2</sub>fused™ patent estate

| Patent family                                             | Granted US patents              | European status | Other granted jurisdictions | Pending    |
|-----------------------------------------------------------|---------------------------------|-----------------|-----------------------------|------------|
| Whipped Formulations                                      | US 11,622,922;<br>US 12,161,737 | In prosecution  | AU, BR, CA, MX              | EP, CN, HK |
| Thermal-Stable Whipped Formulations                       | US 11,826,440                   | In prosecution  | AU, BR, CA, MX              | EP, CN, HK |
| Whipped Formulations (solid or high-viscosity ingredient) | US 11,612,551; US 12,138,332    | In prosecution  | AU, BR, CA, CN, MX          | EP, HK     |

| Patent family                                    | Granted US patents  | European status    | Other granted jurisdictions | Pending |
|--------------------------------------------------|---------------------|--------------------|-----------------------------|---------|
| Whipped Formulations with Desired Sensory Impact | Application pending | EP 3454946 granted | AU, BR, CA, HK, MX          | US, CN  |
| Whipped Gel Formulations                         | US 11,964,035       | EP 3454826 granted | AU, BR, CA, HK              | CN, MX  |

Status is subject to change as applications proceed; current status can be confirmed in the public USPTO and EPO registers.

## 11.2 Layered platform protection

Platform technologies are best protected in layers rather than by a single foundational patent. The eN<sub>2</sub>fused™ estate follows this model, covering the core whipped formulation, specific formulation classes such as gels and high-viscosity systems, performance attributes such as thermal stability and sensory impact, and supporting manufacturing know-how held as trade secrets.

## 11.3 Categories of protection

| Category                            | What it covers                                                                                     |
|-------------------------------------|----------------------------------------------------------------------------------------------------|
| Composition and formulation patents | The formulation itself, or new combinations, ratios, or functional relationships among ingredients |
| Device patents                      | Valve geometries, actuator designs, bag construction, pressure management                          |
| Method-of-manufacture patents       | Mixing sequences, gas incorporation methods, filling technologies, process controls                |
| Method-of-use patents               | New indications, dosing regimens, or application techniques                                        |
| Trade secrets                       | Processing parameters, equipment settings, and know-how not suited to public disclosure            |

### 11.4 Freedom to operate and documentation

Patents do not by themselves guarantee freedom to operate; each product should be assessed against third-party patents and applications. Strong patents also depend on thorough development records of objectives, results, unexpected observations, and engineering rationale. This section is a general overview, not legal advice.

## 12. The eN<sub>2</sub>fused™ Platform: Design Philosophy and Engineering

eN<sub>2</sub>fused™ is an integrated system: an N<sub>2</sub>O-infused formulation, a compressed-air Bag-on-Valve package, and matched valve and actuator components, engineered together and manufactured at commercial scale.

### 12.1 Innovation through integration

Emulsion science, N<sub>2</sub>O whipping, Bag-on-Valve packaging, and rheology are each mature disciplines. The eN<sub>2</sub>fused™ innovation lies in engineering them to work as one system, in particular in holding N<sub>2</sub>O within the formula as a stable microbubble structure under compressed-air pressure and releasing it as a controlled, modest expansion on dispensing.

### 12.2 Beginning with the end user

Development starts with the experience: look, feel, spreadability, speed of the foam-to-film transition, residue, and how the product handles in use. Every technical decision then serves that objective, as the one-handed pediatric diaper rash design shows (Section 9.4).

### 12.3 Five integrated engineering systems

| System                 | Core question                                                                                                                        |
|------------------------|--------------------------------------------------------------------------------------------------------------------------------------|
| 1. Formulation         | Can the N <sub>2</sub> O-infused emulsion survive the full mechanical journey and keep a consistent, fine microbubble structure?     |
| 2. Mechanical delivery | Do the can, bag, valve, and actuator work as one unit in metering and dispensing a quality product?                                  |
| 3. Pressure management | Is the compressed-air charge enough to keep dispensing force appropriate and N <sub>2</sub> O in the product from first use to last? |

| System               | Core question                                                                                             |
|----------------------|-----------------------------------------------------------------------------------------------------------|
| 4. Manufacturing     | Can whipping, N <sub>2</sub> O loading, filling, and charging be reproduced reliably at commercial scale? |
| 5. Human interaction | Does the product feel effortless and correctly dosed to the user?                                         |

None of these systems operates independently. A change in rheology may require a different valve; a different valve may change how the product decompresses; that may change ribbon stability and, ultimately, sensory perception. Optimization must be simultaneous, not sequential.

## 12.4 Managing engineering trade-offs

- **Ribbon stability vs. spreadability:** more structure improves appearance but can make application harder.
- **Richness vs. lightness:** highly structured systems feel luxurious; less structured systems absorb faster.
- **Dispensing speed vs. control:** rapid dispensing is visually dramatic; slower dispensing improves dose control.
- **N<sub>2</sub>O loading vs. structure:** more gas lowers density but can reduce structural integrity and increase agglomeration risk.

In each case the objective is optimization, not maximizing any one characteristic.

## 12.5 Establishing a design space

Mature development defines scientifically justified operating ranges, not a single ideal condition, for mixing energy, N<sub>2</sub>O whipping and loading, fill temperature, compressed-air charge pressure, valve dimensions, and rheological targets. Working within an established design space absorbs normal process variability while keeping performance consistent. Exact values are established experimentally for each product.

## 12.6 Quality by Design applied to the platform

Critical Quality Attributes for the platform may include dispensing consistency, microbubble size and uniformity, sensory performance, evacuation, ribbon stability, and collapse behavior. Critical Process Parameters may include whipping conditions, N<sub>2</sub>O

loading, filling conditions, compressed-air charge pressure, valve assembly, and temperature control.

12.7 Scientific transparency

The most credible innovation claims are those that can be demonstrated experimentally. Platform advantages are explained using established principles of fluid mechanics, rheology, surface chemistry, packaging engineering, and human factors, and supported with data such as the imaging and evacuation results in Section 9.

13. Demonstrating Performance: An Evaluation Framework

Every claim about a delivery system should answer three questions: what changed, how was it measured, and why does it matter? This matters especially for whipped formulations, whose most meaningful advantages are often experiential rather than pharmacological.

13.1 Ask the right comparative question

"Is a whipped formulation better than a cream?" has no meaningful scientific answer. The useful question is: under what conditions does an N<sub>2</sub>O-infused whipped formulation provide measurable advantages over alternative dosage forms? Technologies are rarely universally superior; they are optimized for specific applications.

13.2 Five categories of comparative performance

| Category       | Representative measures                                                                                            |
|----------------|--------------------------------------------------------------------------------------------------------------------|
| Pharmaceutical | Content uniformity, stability, microbiological quality, dose consistency                                           |
| Engineering    | Dispensing force, evacuation, flow characteristics, pressure retention                                             |
| Physical       | Foam density, expansion ratio, microbubble size and uniformity, ribbon stability, collapse behavior, spreadability |
| Consumer       | Sensory preference, ease of application, cosmetic elegance, perceived richness                                     |

| Category   | Representative measures                                                                   |
|------------|-------------------------------------------------------------------------------------------|
| Commercial | Manufacturing reproducibility, scalability, supply chain robustness, regulatory readiness |

### 13.3 Linking instrumental data to human experience

Correlating instrumental measurements with sensory outcomes is one of the biggest opportunities in topical formulation. Lower friction coefficient may correspond with greater perceived silkiness, higher elastic modulus with richer feel, and more uniform bubble size with smoother application. Established correlations let scientists predict consumer response before large sensory studies, which shortens development.

### 13.4 An evidence hierarchy

1. **Engineering characterization:** rheology, foam and bubble analysis, imaging, dispensing metrics
2. **Analytical laboratory studies:** stability, uniformity, packaging compatibility
3. **Controlled sensory evaluations:** trained panels, consumer preference, human factors
4. **Clinical performance studies:** adherence, satisfaction, and therapeutic outcomes, where appropriate and demonstrated rather than assumed

### 13.5 Statistical vs. practical significance

A statistically significant reduction in dispensing force may be imperceptible to consumers, while modest instrumental differences can produce large preference shifts. Sound evaluation combines statistical rigor, engineering judgment, clinical understanding, and consumer insight.

### 13.6 Building credibility through transparency

Confidence grows when endpoints are clearly defined, methods are validated, limitations are reported, comparisons are appropriate, and measured results are kept distinct from interpretation. Technical audiences value candor, and positive findings are more persuasive when limitations are stated openly.

## 14. Troubleshooting Quick Reference

Experienced developers start by asking which scientific principle explains a behavior, not which ingredient to change. The table below is a starting point for that question, not a substitute for structured root-cause investigation.

| Observed symptom                                    | Most likely root-cause categories                                                                                                                                |
|-----------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Spitting or burping on dispensing                   | Microbubble agglomeration into large gas pockets; weak interfacial film; non-uniform whipping; temperature excursions in storage                                 |
| Product foams inside the bag or bag appears swollen | Product pressure too low to hold N <sub>2</sub> O in solution; compressed-air charge loss; late-life pressure decline; excessive N <sub>2</sub> O loading        |
| Whip is weak, flat, or inconsistent between units   | Low or variable N <sub>2</sub> O loading; N <sub>2</sub> O loss through bag film or seals; formula with low N <sub>2</sub> O affinity (low lipid or wax content) |
| Foam collapses immediately after dispensing         | Insufficient yield stress; weak interfacial film; excessive oil loading; poor microbubble retention                                                              |
| Foam excessively rigid or hard to spread            | Excessive yield stress; over-structured polymer system; excessive N <sub>2</sub> O loading                                                                       |
| Whip quality changes late in package life           | Compressed-air pressure falling below what keeps N <sub>2</sub> O and microbubbles compressed; fill-to-can volume ratio too high                                 |
| Flow becomes inconsistent over package life         | Valve restriction or partial blockage; irregular bag collapse; compressed-air pressure loss                                                                      |
| Ribbon twists or forms inconsistently               | Actuator asymmetry; flow imbalance; rheology drift; valve misalignment; bubble agglomeration                                                                     |
| Viscosity decreases during storage                  | Polymer degradation; electrolyte interactions; hydrolysis; microbial contamination                                                                               |

| Observed symptom                                                | Most likely root-cause categories                                                                                                                   |
|-----------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| Phase separation during storage                                 | Insufficient emulsification; droplet coalescence; density mismatch; temperature cycling                                                             |
| Pressure falls over time                                        | Compressed-air leakage at valve, crimp, or seals; seal incompatibility                                                                              |
| Incomplete product evacuation                                   | Bag geometry; product viscosity; bag adhesion; valve placement                                                                                      |
| Batch-to-batch inconsistency                                    | Raw material variability; equipment differences; variation in mixing energy or whipping and N <sub>2</sub> O loading conditions; operator technique |
| Active ingredient degrades faster than in the conventional form | Oxidative interaction with N <sub>2</sub> O; packaging incompatibility; temperature exposure                                                        |
| Consumers perceive the product as greasy                        | Oil selection; surface friction; absorption rate; residual film formation                                                                           |

## 14.1 Structured root-cause tools

- **Five Whys:** repeated questioning that moves past symptoms to the governing process variable.
- **Fishbone (Ishikawa) diagrams:** sort causes into materials, methods, machines, measurement, personnel, and environment.
- **Pareto analysis:** focuses effort on the few recurring causes behind most issues.
- **FMEA:** rates severity, occurrence, and detectability to drive proactive risk reduction.
- **CT imaging:** non-destructive view of microbubble structure inside a filled package, useful for confirming agglomeration (Section 9.3).

## 14.2 Common development mistakes to avoid

- Beginning with ingredients rather than user needs
- Optimizing the formulation before selecting the delivery platform
- Treating N<sub>2</sub>O loading and air charge pressure as fixed rather than as design variables
- Ignoring human factors until commercialization

- Treating packaging as a purchasing decision instead of an engineering decision
- Assuming laboratory success guarantees manufacturing success
- Optimizing one parameter while degrading overall system performance

## 15. Future Directions

The next generation of topical innovation is likely to come from system-level engineering rather than isolated improvements to one ingredient or component.

- **AI and predictive formulation:** machine learning on QbD datasets may reveal nonlinear interactions among formulation, N<sub>2</sub>O loading, and process variables, augmenting rather than replacing formulation scientists.
- **Digital twins and computational fluid dynamics:** CFD is particularly relevant to valve and actuator design and to modeling microbubble expansion at the orifice, which could reduce prototype iterations.
- **Human-centered design:** delivery systems that adapt to users with arthritis, limited dexterity, or pediatric needs, rather than expecting users to adapt.
- **Sustainable engineering:** material reduction, recyclability, and packaging free of liquid hydrocarbon propellants, balanced with safety, stability, and regulatory requirements.

## 16. Conclusion

Whipped formulation technology is more than a packaging innovation. The eN<sub>2</sub>fused™ platform integrates an N<sub>2</sub>O-infused formulation, a compressed-air Bag-on-Valve package, and precision dispensing components into one engineered system. It is proven in commercial products, protected by granted patents, and recognized by industry innovation awards.

Great topical products are not created by optimizing a formulation alone. They come from engineering every interaction between the formula, the gas, the package, and the person who uses it.

### 16.1 Working with Formulated Solutions

Brand owners and development partners exploring whipped delivery can expect a structured path:

1. Opportunity assessment against the selection criteria in Section 8.7
2. Placebo whipping and Bag-on-Valve compatibility trials

3. Valve, actuator, N<sub>2</sub>O loading, and pressurizing optimization
4. API stability assessment and functional testing
5. Scale-up and commercial manufacturing

## Appendix: Glossary of Key Terms

| Term                              | Definition                                                                                                                                                                                                                                        |
|-----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Bag-on-Valve (BoV)                | Dispensing technology in which product is held in a flexible bag attached to the valve, with compressed gas (in eN <sub>2</sub> fused™, compressed air) between the bag and the can squeezing the bag to dispense. Contains no liquid propellant. |
| Coalescence                       | Permanent merging of emulsion droplets, irreversibly reducing interfacial area                                                                                                                                                                    |
| Collapse profile                  | The engineered transition of a dispensed whipped product from expanded foam into a spreadable film                                                                                                                                                |
| Compressed-air charge             | The air sealed between the bag and the can that provides the dispensing force; its pressure declines as the bag empties                                                                                                                           |
| Critical Material Attribute (CMA) | A raw material property, such as polymer molecular weight or N <sub>2</sub> O grade, that may affect one or more CQAs                                                                                                                             |
| Critical Process Parameter (CPP)  | A manufacturing parameter, such as mixing energy, N <sub>2</sub> O loading, or air charge pressure, that affects one or more CQAs                                                                                                                 |
| Critical Quality Attribute (CQA)  | A property that must stay within defined limits to ensure quality, such as assay, yield stress, or ribbon formation                                                                                                                               |
| Design space                      | The combination of input variables and process parameters demonstrated to yield acceptable quality                                                                                                                                                |

| Term                                  | Definition                                                                                                                                                                                                                                                       |
|---------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Expansion ratio                       | How much compressed gas bubbles in the product expand on release to atmospheric pressure; about 1 to 6 times for eN <sub>2</sub> fused™ N <sub>2</sub> O microbubbles, versus roughly 120 times for liquefied hydrocarbon propellant changing from liquid to gas |
| Extractables / leachables             | Compounds removable from packaging under aggressive test conditions (extractables) versus those that actually migrate into product during normal storage (leachables)                                                                                            |
| Functional stability                  | Whether a product continues to dispense, whip, and collapse as designed; separate from chemical stability                                                                                                                                                        |
| Microbubble agglomeration             | Merging of fine N <sub>2</sub> O microbubbles into larger gas pockets inside the package; a cause of coarse foam, spitting, and burping                                                                                                                          |
| N <sub>2</sub> O infusion             | Whipping nitrous oxide into the formulation before filling so it saturates the formula and is held as fine microbubbles under pressure                                                                                                                           |
| Product evacuation                    | The percentage of product dispensed from a package during normal use                                                                                                                                                                                             |
| Quality by Design (QbD)               | A development approach that designs quality in from the outset rather than testing for it afterward                                                                                                                                                              |
| Quality Target Product Profile (QTPP) | A prospective summary of the clinical, pharmaceutical, performance, and commercial characteristics a product must achieve                                                                                                                                        |
| Yield stress                          | The minimum force required to start a formulation flowing; a key driver of ribbon formation and foam stability                                                                                                                                                   |